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FUNCTIONAL CHANGES IN THE BRAIN OF THE DOG AFTER REDUCTION OF THE CEREBRAL BLOOD SUPPLY

II. DISTURBANCES OF CONDITIONED REFLEXES AFTER LIGATION OF ARTERIES

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As was mentioned in paper I of this series,[1] acute anemia resulting from complete or partial restriction of the cerebral circulation produces temporary or permanent disturbances of higher nervous activity. Loss of intelligence after ligation or temporary compression of the main arteries supplying the brain was observed in different animals (dogs, cats, monkeys and others) by Cooper[2] (1836), Hill[3] (1900), Pike, Guthrie and Stewart[4] (1906), Crile and Dolley[5] (1908), Gildea and Cobb[6] (1930) and others. Usually these disturbances were temporary and were noted in the first hours or days of the anemic condition. When the animals were observed longer, most of the authors believed that they recovered completely. It is difficult, however, to judge of the full restoration of the mental processes in animals. Under laboratory conditions these animals manifest all the functions normal to the ordinary animal, although the finest processes of higher nervous activity may

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have been destroyed. Many experiments in Pavlov's laboratory showed that after excision of a large part of the cortex in the dog entire restoration of its elementary functions was often observed but the delicate processes of analysis and synthesis were irremediably destroyed.

The aim of the present study was to investigate the changes in higher nervous activity by the method of conditioned reflexes in dogs after ligation of four or more of the arteries supplying the brain. Four dogs were studied thus, two of them having a permanent fistula of the parotid gland.

METHOD

Conditioned reflexes were established, either the motor or the salivary reaction being used as an indicator.

Conditioned motor reflexes were established in the following ways. In response to a positive stimulus the dog had to make a complicated motor reaction; i. e., it had to mount a ladder about 4½ feet long to a platform where it received food. The conditioned reflex was delayed for twenty seconds; i. e., if during twenty seconds of application of the stimulus the conditioned motor reaction did not appear, the dog received food on the platform. The animal had to mount to the platform during the action of the positive stimulus. The negative stimuli were never reenforced by food. The motor reaction to the negative stimulus was correct if the dog either sat quiet and did not move, or got up and walked about the room but did not mount to the platform. When the dog mounted to the platform in error (i. e., responded positively to the negative stimulus), it received no punishment but was not given food. The experiments with the conditioned motor reactions were carried out in a large room in which the dog could move about freely. The experimenter was isolated from the dog by a screen.

All the conditions necessary for the study of conditioned salivary reflexes were strictly fulfilled. During the experiment the dog was in a sound-proof room, isolated from the experimenter, and was observed only through a periscope. By means of a special system of suction pipes and a water manometer the secretion of saliva was recorded and measured on a scale, two divisions of the scale being equal to 1 drop of saliva. The conditioned stimuli were applied from the observation room only, and the feeding of the dog during the experiment was carried out automatically. The conditioned salivary reflexes were established by means of the unconditioned alimentary reflex. The magnitude of the conditioned response was measured by the quantity of saliva secreted in thirty seconds when the conditioned stimulus was acting alone; positive stimuli were reenforced immediately thereafter by the offering of food.

Ligation of the arteries was performed in two dogs (no. 4 and no. 8) before the beginning of the experiments with conditioned reflexes. In two other dogs (no. 24 and no. 23) the vessels were tied after the normal activity of the brain had been studied by the method of conditioned reflexes. The vessels were tied in different combinations over different intervals of time. One month or six weeks after the last operation the animal was killed. An opaque substance was injected into the arterial system and a detailed roentgen and anatomic examination was made (paper I).

PROTOCOLS

Dog 4.—The animal was operated on at the age of 1½ months. Both carotid and both vertebral arteries were tied simultaneously in the neck (paper I, table 1). With this dog the effect of the ligation of four arteries on the higher

nervous activity in the young animal was studied, i. e., during the period of growth of the organism and development of its intelligence. Experiments were continued for twenty-two months, after which the animal was killed. A year after the beginning of the work on this dog a permanent parotid fistula was established, and the conditioned salivary reflexes were studied. This made it possible to compare the two methods of investigation, i. e., that of motor and that of salivary conditioned reflexes, respectively. The establishment of motor and salivary conditioned reflexes proceeded normally. Positive conditioned reflexes were obtained without particular difficulty to the following stimuli: the beating of a metronome at a rate of 120 beats per minute, the ringing of an electric bell, the sound of a buzzer, the lighting of an electric bulb, tactile stimulation of the skin of the left thigh, the appearance of a circle on a screen and tones of 100, 1,000 and 1,800 cycles per second produced by a low frequency oscillator (type 377 B, General Radio Company, Cambridge, Mass.). The animal was then trained to differentiate from these stimuli the following negative stimuli, which were never reenforced by food: the beating of a metronome at a rate of 60 beats per minute, tones of 300 and 25,000 cycles per second, tactile stimulation of the skin of the left shoulder and the appearance of a square on a screen. The tone of 500 cycles per second was used as a conditioned inhibitor of the normally positive response to tactile stimulation. The combination of the tone of 500 cycles per second with tactile stimulation was never reenforced by food. The inhibitory process was also studied on several occasions by "acute" extinction of the positive response to the tone of 1,000 cycles per second and an electric bell. That is to say, this stimulus was given repeatedly at three minute intervals without reenforcement by food until the conditioned reflex had completely disappeared on two successive trials. A long delayed conditioned reflex was established to the buzzer. In this case the duration of the isolated application of the buzzer was sixty seconds; after this the dog received food. The delayed conditioned reflex is well established when the salivary secretion or motor reaction finally settles at a definite intermediate position between the commencement of the conditioned stimulus and its reenforcement with food.

The general behavior of this dog was in sharp contrast to the behavior of normal laboratory dogs. At the end of the investigation the dog was 2 years old; in spite of this, its behavior remained like that of a puppy. The dog learned with difficulty to find the experimental room unaided. A normal dog can do this after very little experience. Any slight change in the surroundings inhibited the animal absolutely. For instance, if some unaccustomed object was encountered on the way to the experimental room—a sheet of paper or other object—it was sufficient to deter the dog from going farther. The experimenter had to drag the animal by the collar, while it evinced signs of fear, trembled, resisted and bit. When free the dog was always excited and often misjudged its surroundings and knocked against objects. When it hurt itself it lay down immediately and remained in the same position until the experimenter came to it. The usual excitement quickly changed to sleep during the experiment. While solving some difficult problem during the experiment the dog was highly excited, but the excitement quickly changed to deep inhibition and the dog fell asleep. All these disturbances were increased after a second operation; so work with this dog was very difficult.

The elementary activity of the cortex, as expressed in the state of the conditioned reflexes, was not disturbed in this dog. The establishment of positive conditioned reflexes and rough differentiations did not show any changes. When I began, however, to establish a differentiation between the beating of a metronome at a rate of 100 beats per minute and a positive stimulus of 120 beats per minute

after a period of excitement, at the first trials inhibition and sleep came on. It was necessary to take special precautions in order to obtain a differentiation of this stimulus. The negative stimulus was tried not more than once during an experiment and only every other day. The attempt to obtain a more delicate differentiation between the positive stimulus of 120 beats per minute and a negative stimulus of 110 beats was a complete failure and resulted in the disappearance of other conditioned reflexes. With other dogs under the same experimental conditions discrimination between 120 and 118 metronome beats per minute was obtained (table 1).

Great difficulties were also encountered in the establishment of a long delayed conditioned motor reaction when the feeding was postponed for ninety seconds

TABLE 1.—*The State of the Conditioned Motor Reaction in Dog 4 After Application of a Negative Stimulus (Beating of a Metronome at a Rate of 110 Beats per Minute)*

Time	Conditioned Stimulus*	Serial No. of Application of Stimulus	Conditioned Motor Reaction: Latent Period, Seconds	Conditioned Motor Reaction: Duration of Reaction, Seconds	Comment
28/11/32, p.m.					Experiment 204
4:47	Metronome, 120....	699	1	4	
4:52	Electric light.....	25	1	3	Dog lying in center of room; got up and mounted quickly to the platform
4:56	**Metronome, 100 †..**	**121**	..	..	Lay quietly; did not get up
4:58	Electric light.....	26	1	3	Stood up and mounted quickly to platform
5:01	**Metronome, 120...**	700	3	6	Lying down; stood up after three sec.; mounted to platform after six sec.
5:04	**Metronome, 110...**	**21**	10	..	Stood up after ten sec.; excited; walked around the room; did not mount to platform
5:10	Electric light.....	27	1	..	Up immediately; excited; ran around the room; did not mount to the platform; food was given after 20 sec.; excitement stronger; ran around more quickly; did not mount during sixty sec.; dragged by the collar up on to platform; ate very well
5:15	Electric bell.....	661	1	..	Same reaction as previous one; did not mount to platform

* The negative stimuli in this and other tables are printed in bold face type.
† Beats per minute, in this and all other tables.

after the beginning of the conditioned stimulus (sound of a buzzer). Under normal conditions the conditioned motor reaction begins in the second half of this period; i. e., the dog mounts the platform from forty-five to fifty-five seconds or even more after the buzzer begins to sound. The buzzer stimulus was tried one hundred and forty-three times, but the conditioned reflex delayed for ninety seconds was not established. The dog was so deeply inhibited that it would not mount the platform even when the food was given or placed on the platform. The conditioned motor reaction to other stimuli also disappeared during this period. The dog fell asleep during the experiment. Thus the animal again failed to solve this difficult problem.

After a year's work on conditioned motor reactions, conditioned salivary reflexes were established in this dog. The attempt to obtain the delayed conditioned reflex was repeated under new conditions. The conditioned reflex to the sound of a buzzer was delayed for sixty seconds. The buzzer stimulus was tried

fifty times in this series of experiments. In nine trials only did the salivary secretion begin after thirty seconds; in the rest of the trials it began much sooner. The delayed salivary reflex was established, but it was unstable and very often did not appear.

After the formation of positive and negative conditioned salivary reflexes and the determination of the highest limit of hearing, the second operation was performed. On Oct. 24, 1933, the following arteries were tied and cut on the right side: common carotid (just below the origin of the superior thyroid artery), superior thyroid, internal and external carotid and occipital. The parts of the arteries between the ligatures were excised. After this operation there were no changes in the general behavior of the animal, but pronounced inhibition was observed during the experiments with conditioned reflexes.

TABLE 2.—*Conditioned Reflexes in Dog 4 Before and After the Second Operation*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Salivary Reaction		Comment
			Latent Period, Seconds	Secretion, Scale Division of Manometer	
13/9/33					Experiment 78 (before second operation)
12:20 p.m.	Light.....	92	4	26	
12:26 p.m.	Tactile.....	136	4	10	
12:32 p.m.	Metronome, 120....	39	5	35	
12:37 p.m.	Tone (1,000 c.p.s.)*	84	9	11	
12:44 p.m.	Tone (100 c.p.s.)...	54	7	16	
12:49 p.m.	Tactile.....	137	3	22	
12:55 p.m.	Tone (18,000 c.p.s.)	43	2	29	
1:00 p.m.	Electric bell.....	20	3	25	
11/11/33					Experiment 120 (after second operation)
11:31 a.m.	Light.....	137	13	8	Dog drowsy during experiment
11:36 a.m.	Tactile.....	190	27	2	
11:42 a.m.	Tone (1,000 c.p.s.).	78	20	5	Asleep
11:48 a.m.	Tone (18,000 c.p.s.)	68	..	traces	
11:53 a.m.	Metronome, 120....	59	14	7	
11:57 a.m.	Circle.....	66	21	2	
12:04 a.m.	Light.....	138	..	traces	

* In this and other tables cycles per second is represented by c.p.s.

Table 2 shows the protocols of two experiments, 78 and 120, the former carried out before and the latter eighteen days after the second operation. The magnitude of the conditioned reflex was seen to be decreased and the latent period to be prolonged in experiment 120.

In experiment 113 (table 3) the dog fell asleep after the application of the inhibitory stimulus (appearance of a square). The inhibition was increased still more by the delayed conditioned stimulus (sound of a buzzer). At the end of this experiment the conditioned reflexes had disappeared.

The third operation was performed on Nov. 14, 1933. The left vertebral artery and its terminal branches were tied and cut at the back of the neck between the first and the second vertebra. After this operation the state of the conditioned reflexes was not noticeably changed. The fourth operation was performed two weeks later. The same arteries were tied as in the third operation, but on the right side. All conditioned reflexes disappeared in the first six days after this

operation. The dog was healthy and ate the food greedily, and the wound healed by first intention. The state of the conditioned reflexes five days after the fourth operation is shown in table 4. A very weak conditioned reflex was obtained in response to tones of 100 and 1,000 cycles per second. The strong conditioned stimulus (ringing of an electric bell) was ineffective. During the experiment there was inhibition, passing into sleep. On the tenth day after the operation the differentiations (appearance of a square and tone of 25,000 cycles per second) were tried (table 5). As may be seen in table 5, the discrimination of a square from a circle and that of the positive tone of 1,800 cycles per second from the

TABLE 3.—*Conditioned Reflexes in Dog 4 Ten Days After the Second Operation*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Salivary Reaction: Latent Period, Seconds	Conditioned Salivary Reaction: Secretion, Scale Division of Manometer	Comment
4/11/33					Experiment 113
11:37 a.m.	Light	128	13	5	
11:44 a.m.	Circle	60	24	3	
11:53 a.m.	Circle	61	13	3	Dog drowsy
11:58 a.m.	**Square**	**16**	**0**	**0**	
12:03 p.m.	Circle	62	0	0	Asleep
12:09 p.m.	Metronome, 120	49	16	10	
12:15 p.m.	Buzzer (delayed reflex, sixty sec.)	55	38	0-0-4-6	Long delayed conditioned reflex
12:19 p.m.	Metronome, 120	50	0	0	Drowsy
12:23 p.m.	Circle	63	0	0	Drowsy

TABLE 4.—*Conditioned Reflexes in Dog 4 Five Days After the Fourth Operation*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Salivary Reaction: Latent Period, Seconds	Conditioned Salivary Reaction: Secretion, Scale Division of Manometer	Comment
3/12/33					Experiment 133
1:02 p.m.	Light	153	0	0	Dog ate greedily
1:08 p.m.	Tone (100 c.p.s.)	69	10	2	Drowsy
1:14 p.m.	Tone (100 c.p.s.)	70	0	0	
1:19 p.m.	Tone (1,000 c.p.s.)	96	26	3	
1:24 p.m.	Circle	76	0	0	
1:30 p.m.	Electric bell	28	0	0	
1:36 p.m.	Light	154	0	0	

negative tone of 25,000 cycles per second were obtained. After the application of the inhibitory stimuli a very strong after-effect of inhibition was observed.

The fifth operation was performed on Dec. 12, 1933. The same arteries were tied on the left side as were tied on the right side in the third operation. The state of the conditioned reflexes on the sixth and twenty-fifth days after the last operation is seen in tables 6 and 7, respectively. The conditioned reflexes were very weak. There was drowsiness during the experiment. The conditioned inhibitory tone of 500 cycles per second plus a tactile stimulus and differentiation on tactile irritation of the skin retained their inhibitory effect. The discrimination of tones of 25,000 and 300 cycles per second from the positive tones of 18,000 and 1,000 cycles per second was lost and had not reappeared at the end of the investigation. The response to the buzzer (reflex delayed for sixty seconds) was completely disinhibited, as

is shown in table 7. The highest limit of hearing, which had been 37,000 cycles per second, fell to 30,000 cycles per second and did not return to normal. The increase in the inhibitory process was as pronounced in the experiments with extinction. After the first operation, to obtain complete extinction of the conditioned reflex to the tone of 1,000 cycles per second it was necessary to repeat the tone six times without giving food. After the second operation extinction was obtained after four trials; after the third operation, after three trials (table 12). The dog was killed thirty days after the last operation.

TABLE 5.—*Conditioned Reflexes and Differentiations in Dog 4 Ten days After the Fourth Operation*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Salivary Reaction: Latent Period, Seconds	Conditioned Salivary Reaction: Secretion, Scale Division of Manometer	Comment
8/12/33					Experiment 136
12:39 p.m.	Light.....	158	20	3	
12:44 p.m.	Circle.....	79	8	9	
12:50 p.m.	**Square**.....	**19**	**0**	**0**	
12:55 p.m.	Circle.....	80	0	0	Drowsy
1:00 a.m.	Tone (1,000 c.p.s.).....	99	20	1	
1:06 a.m.	Tone (18,000 c.p.s.).....	88	20	5	Drowsy
1:13 a.m.	**Tone (25,000 c.p.s.)**....	**22**	**0**	**0**	
1:18 a.m.	Tone (18,000 c.p.s.).....	89	0	0	Asleep
1:22 a.m.	Circle.....	81	8	14	
1:27 a.m.	Tone (18,000 c.p.s.).....	90	17	10	Drowsy

TABLE 6.—*Conditioned Reflexes in Dog 4 Six Days After the Fifth Operation*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Salivary Reaction: Latent Period, Seconds	Conditioned Salivary Reaction: Secretion, Scale Division of Manometer	Comment
18/12/33					Experiment 140
1:28 p.m.	Light.....	162	8	6	Quiet and drowsy during the experiment; took food, however, immediately
1:33 p.m.	Tactile.....	304	7	6	
1:38 p.m.	Tone (1,000 c.p.s.).....	112	4	18	
1:44 p.m.	Tone (18,000 c.p.s.).....	93	5	17	
1:51 p.m.	Metronome, 120.....	71	8	7	
1:56 p.m.	Light.....	163	0	0	

The development of vascular collateral passages and anastomoses in this dog as a result of the ligation of ten main arteries has been described in paper I of this series. The disturbances in the cortical activity after restriction of the cerebral circulation in this animal may be summarized as follows: (1) a distinct strengthening of inhibition with drowsiness passing into deep sleep, especially after application of negative stimuli; (2) disappearance of conditioned reflexes during the first six days after the ligation of the arteries; (3) after the reappearance of the conditioned reflexes absence of the ability to discrimnate between the negative stimuli (tones of 300 and 25,000 cycles per second) and the positive stimuli (tones of 100 and 18,000 cycles per second). These disturbances, however,

were temporary; from ten to twelve days after the operation the animal could again discriminate the tones, but this faculty disappeared permanently after the fifth operation. The upper limit of hearing had at the same time been reduced from 37,000 to about 30,000 cycles per second. After the fifth and last operation the dog remained under observation for one month; in this period a return to normal occurred, that is, to the condition in which the dog was before the second operation. The conditioned reflexes were better, but the disturbances of the acoustic analyzer remained constant.

Dog 8.—This dog was operated on at the age of 2½ months The following arteries were tied and cut: the subclavian, common carotid and vertebral and the costocervical and omocervical trunks on the right side. After the operation symptoms of severe cortical and bulbar disturbances occurred during three days. Six days after the ligation of the arteries the training of the dog for conditioned motor reactions was begun. During seventeen months of this work no

Table 7.—*Conditioned Reflexes in Dog 4 Twenty-Five Days After the Fifth Operation*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Salivary Reaction: Latent Period, Seconds	Conditioned Salivary Reaction: Secretion, Scale Division of Manometer	Comment
6/1/34					Experiment 147
1:14 p.m.	Light.....	170	6	7	
1:22 p.m.	Tone (18,000 c.p.s.).....	103	13	5	
1:27 p.m.	Tone (25,000 c.p.s.)...	26	8	5	
1:32 p.m.	Tone (18,000 c.p.s.).....	104	23	1	Drowsy
1:36 p.m.	Tone (1,000 c.p.s.).....	125	8	11	
1:45 p.m.	Buzzer (reflex delayed sixty sec.)	64	6	4-1-2-3	Long delayed conditioned reflex completely disinhibited; secretion noted every fifteen sec. during one min.
1:50 p.m.	Metronome, 120.....	75	27	3	Drowsy; slept
1:57 p.m.	Electric bell.....	35	9	7	

particular changes were observed in the higher nervous activity of this dog. The first conditioned motor reflex (i. e., to the beating of the metronome at a rate of 120 beats per minute) was established after fifty trials. A conditioned motor reaction was established to the following stimuli after five trials: the ringing of an electric bell, the sound of a buzzer, the lighting of an electric lamp and the tone of 512 cycles per second produced by a harmonium. The differentiation of the beating of a metronome at a rate of 60 from the positive stimulus at a rate of 120 was complete after twenty-six trials. Full discrimination between the negative stimulus at a rate of 110 and the positive stimulus at a rate of 120 was obtained after nine trials. After this the training for more delicate differentiations of 114 and 118 beats per minute was begun. As may be seen from table 8, this discrimination was obtained. The differentiation of beating of a metronome at a rate of 118 was evidently the limit of discrimination. It was unstable, and after its application a very strong "after-effect" inhibition developed, so that the conditioned motor reaction to beating at a rate of 120 was completely inhibited and the dog became drowsy. The discrimination of a strong light (positive stimulus) from a weak light (negative stimulus) was obtained after ten trials. This differentiation was absolute. Complete discrimination was also obtained of

tones of 325 and 488 cycles per second from the positive tone of 512 cycles per second. These differentiations were stable after eleven trials.

The training for a long delayed conditioned reflex was then started. The reaction to the conditioned stimulus (sound of a buzzer) was delayed for two

TABLE 8.—*State of Differentiations in Dog 8*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Motor Reaction, Seconds	Comment
9/11/32				Experiment 74
5:44 p.m.	Electric bell.....	95	2	Sitting at ladder; immediately stood up
5:46 p.m.	Buzzer.....	36	3	
5:49 p.m.	**Metronome, 110**.....	**31**	**0**	Lying on floor; did not get up
5:51 p.m.	Metronome, 120.....	362	5	Sitting at ladder; stood up after four sec.
5:55 p.m.	Metronome, 120.....	363	5	
5:58 p.m.	**Metronome, 114**.....	**29**	**0**	Sitting near ladder; did not get up
6:01 p.m.	Metronome, 120.....	364	4	Stood up after three sec.
6:05 p.m.	Metronome, 120.....	365	5	
6:09 p.m.	**Metronome, 118**.....	**2**	**0**	Sitting quietly; did not get up; scratched itself
6:11 p.m.	Metronome, 120.....	366	5	
6:14 p.m.	Metronome, 120.....	367	5	
6:18 p.m.	**Metronome, 118**.....	**3**	**19**	Stood up after eighteen sec.; mounted to platform after nineteen sec.
6:23 p.m.	Metronome, 120.....	368	4	

TABLE 9.—*Delayed Conditioned Motor Reaction in Dog 8 After the Ninetieth Trial*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Motor Reaction		Comment
			Latent Period, Seconds	Duration, Seconds	
14/10/33					Experiment 191
5:16 p.m.	Light.....	89	1	2	Sitting at ladder; stood up after one sec.; mounted immediately
5:21 p.m.	Tone (512 c.p.s.).....	44	1	3	
5:23 p.m.	**Tone (324 c.p.s.)**.....	**15**	**2**	**0**	Stood up after two sec.; walked about; did not mount
5:26 p.m.	Tone (512 c.p.s.).....	45	1	3	
5:29 p.m.	Metronome, 120.....	608	3	5	
5:34 p.m.	Buzzer (reflex delayed 120 sec.)	91	58	93	Lay quietly; stood up after fifty-eight sec.; walked about; mounted after ninety-three sec.
5:41 p.m.	Light.....	90	1	3	
5:43 p.m.	Electric bell.....	224	1	2	

minutes; i. e., the dog did not receive food until two minutes after the buzzer began to sound. The delayed conditioned reaction was established after eighty-one trials. Experiment 191 (table 9) shows the state of the delayed motor reaction after ninety-one trials. As may be seen from the table, the motor reaction started fifty-eight seconds after the buzzer began to sound. The dog mounted to the platform at the ninety-third second. In further experiments with this long delayed conditioned reflex the motor reaction began on the average at the sixtieth second after the buzzer began to sound.

During the seventeen months of this work no particular changes in the higher nervous activity of the dog were observed. The animal solved difficult problems easily, for instance, the discrimination between beating of a metronome at a rate of 120 and that at rates of 114 and 118 or the formation of a conditioned reaction delayed for two minutes. The general behavior of the dog remained normal; it was lively and never slept during the experiments.

The common carotid and vertebral arteries were tied and cut on the left side of the neck seventeen months after the first operation. The conditioned motor reaction disappeared at first and reappeared on the seventh day after the second operation. The discrimination of the tones of 325 and 488 cycles per second from

TABLE 10.—*Conditioned Motor Reaction and Differentiations in Dog 8 Sixteen Days After the Second Operation*

Time	Conditioned Stimulus	Serial No. of Application of Stimulus	Conditioned Motor Reaction: Latent Period, Seconds	Conditioned Motor Reaction: Duration, Seconds	Comment
16/12/33					Experiment 212
9:01 a.m.	Metronome, 120.....	644	1	2	Sitting at ladder; stood up after one sec. and mounted after two sec.
9:04 a.m.	Light.....	126	1	3	
9:07 a.m.	**Light, weak**.....	**20**	**0**	**0**	Lying quietly; did not get up
9:17 a.m.	Light.....	127	1	3	
9:22 a.m.	Metronome, 120.....	645	2	3	
9:25 a.m.	**Metronome, 100**.....	**23**	**0**	**0**	Lying quietly; did not get up
9:27 a.m.	Metronome, 120.....	646	3	5	
9:30 a.m.	Tone (512 c.p.s.).....	90	1	3	
9:33 a.m.	**Tone (488 c.p.s.)**.....	17	**3**	**0**	Lying quietly; stood up after three sec. and walked about; did not mount
9:43 a.m.	Tone (512 c.p.s.).....	91	1	3	Drowsy
9:47 a.m.	Metronome, 120.....	647	1	3	
9:51 a.m.	Buzzer (reflex delayed 120 sec.)	111	8	80	Lying quietly; got up slowly after eight sec.; walked about; after eighty sec. mounted to platform; stayed there till food was given
9:57 a.m.	Electric bell.....	284	1	3	

the positive tone of 512 cycles per second disappeared. The differentiation of a weak light remained without change. The motor reaction to positive stimuli was delayed, and, instead of the normal interval of from two to three seconds, the latent period was increased to from ten to twelve seconds. Table 10 illustrates the state of the conditioned motor reaction and the differentiations sixteen days after the second operation. Differentiations of a weak light, beating of a metronome at a rate of 100 and a tone of 488 cycles per second were complete.

Three weeks after the second operation the third operation was performed; both vertebral arteries and their terminal branches were tied and cut at the back of the neck. A month later the fourth and last operation was performed, the common carotid, occipital, internal and external carotid arteries and the posterior auricular arteries on both sides being tied and cut. The conditioned motor reaction disappeared during the six days following each of the last operations.

Drowsiness during the experiment was increased. All differentiations disappeared at first, but after two weeks they were reestablished except for the differentiation of the tone of 488 cycles per second. Discrimination of the tone of 488 cycles per second from the positive tone of 500 cycles per second had not been established at the end of the work on this dog. The state of the conditioned motor reaction fifteen days after the last operation is shown in table 11. In this experiment the tone of 488 cycles per second was tried twice without any discrimination on the part of the dog.

The dog was killed twenty-one days after the last operation. The general results after ligation of the arteries in this dog were approximately the same as

TABLE 11.—*Conditioned Motor Reaction and Differentiations in Dog 8 Fifteen Days After the Fourth Operation*

Time	Conditioned Stimulus	Conditioned Motor Reaction: Serial No. of Application of Stimulus	Conditioned Motor Reaction: Latent Period, Seconds	Conditioned Motor Reaction: Duration, Seconds	Comment
3/1/33, a.m.					Experiment 225
9:40	Tone (512 c.p.s.).....	127	1	3	Sitting quietly; stood up after one sec.; mounted to platform after three sec.
9:44	Metronome, 120.....	66	1	3	
9:49	**Light, weak**.....	**25**	**0**	**0**	Lying quietly; did not stand up
9:53	Light, strong.....	149	1	5	Drowsy
9:59	Tone (512 c.p.s.).....	128	1	3	
10:05	**Tone (488 c.p.s.)**.....	**33**	**1**	**3**	Lying quietly; stood up after one sec.; mounted to platform after three sec.
10:09	Tone (512 c.p.s.).....	129	1	4	Drowsy
10:12	**Tone (488 c.p.s.)**.....	**34**	**1**	**4**	Stood up immediately; mounted after four sec.
10:17	Tone (512 c.p.s.).....	130	1	3	
10:23	Electric bell.....		**1**	5	Drowsy
10:27	Light, strong.....	150	1	4	
10:33	Buzzer (reflex delayed 120 sec.)	120	13	62	Drowsy; lay quietly; stood up after thirteen sec.; walked about; mounted after sixty-two sec.
10:38	Metronome, 120.....	667	2	4	

with the first dog. Increased inhibition and drowsiness were pronounced in this dog, although they did not reach such a degree as in the first dog.

DOG 24.—In this dog the establishment of the conditioned motor reaction was effected before ligation of the arteries. Experiments were begun when the dog was 1½ months of age and continued for one year. This dog was used for control experiments. The conditioned motor reaction was established to the same positive and negative stimuli as in dog 8. The delayed conditioned motor reaction was formed to the sound of the buzzer and was delayed for thirty seconds. The tone of 870 cycles per second was the conditioned inhibitor to the positive stimulus of an electric light (strong); i. e., the combination of tone plus electric light was never reenforced.

When the investigation of the normal cortical activity had been completed, the dog was operated on. During the first operation (Nov. 3, 1933) both common

carotid arteries and the left vertebral artery were tied and cut. The first experiment was performed five days after this operation. The conditioned motor reaction to the positive stimuli was normal, but the differentiation of beating of a metronome at a rate of 100 and the long delayed conditioned reaction to the buzzer were disinhibited. After thirteen days, however, the differentiation of beating of a metronome at a rate of 100 (negative stimulus) from that at a rate of 120 (positive stimulus) was completely restored, and the general behavior of the dog was the same as before operation.

Two weeks after the first operation, a second operation was performed (Nov. 17, 1933). Both vertebral arteries were tied and cut at the back of the neck. The long delayed conditioned reaction to the buzzer disappeared; the dog did not mount to the platform at all. The discrimination of beating of a metronome at a rate of 100 from the positive stimulus at a rate of 120 was absent. After a trial of any differentiation such as strong after-effect inhibition set in that the conditioned motor reaction to the positive stimuli was completely inhibited.

After the second operation the dog was observed during two weeks. During this period definite changes in the general behavior of the animal were observed. This dog, which had always been lively and excited during the experiments, now became apathetic and drowsy and often fell asleep. The changes in the higher nervous activity were the same as in dog 8. It must be especially remarked that the severe disturbances appeared after the second operation, when both vertebral arteries were tied at the back of the neck. The dog died during the third operation from an accidental cause not connected with the ligation of the arteries.

Dog 23.—With dog 23, conditioned salivary reflexes were established before the ligation of the arteries. Particular attention was given to the study of the auditory capacity in this dog. Conditioned reflexes were established to different tones of from 100 to 30,000 cycles per second, and the highest limit of hearing was determined. Tones of 300 and 19,000 cycles per second and beating of a metronome at a rate of 60 were made negative by differentiation of them from corresponding positive stimuli. The conditioned inhibitor was formed from the tone of 500 cycles per second. When this tone was combined with the positive stimulus (viz., tactile irritation of the skin) the conditioned salivary reflex was completely inhibited. The conditioned salivary reflexes were stable and varied little in magnitude. The differentiations were stable also.

After the training was completed the first operation was performed, both common carotid arteries and the left vertebral artery being tied and cut (paper I, table 1). After the first operation no changes in the positive and negative conditioned reflexes were observed. Three weeks later the second operation was performed. Both common carotid arteries were tied and cut above the origin of the superior thyroid artery; both internal and both external carotid arteries and both occipital arteries were tied and cut. The parts of the arteries between the ligatures were excised. Immediately after the operation sopor was observed, which continued for two days. Strong retraction of the eyes into their orbits (enophthalmos) and ptosis of the third eyelid were also noted. The conditioned reflexes were not reestablished until the sixth day after the operation. The magnitude of the conditioned reflexes was greatly decreased, the latent period was lengthened, and there was pronounced drowsiness during the experiments. Seventeen days after the second operation both vertebral arteries and their terminal branches at the back of the neck were tied and cut.

After the third operation severe disturbances appeared. For the first two days after the operation there was strong panting; then this lessened and appeared

only during movement. When attempting to walk the dog would fall, lie unconscious for some seconds and then slowly stand up. The dog could not eat standing without being supported. Sometimes epileptiform convulsions were observed. These attacks were at first frequent. They were preceded by a syndrome of whining, licking of the lips, breathlessness, enophthalmos, ptosis of the third eyelid and dilatation of the pupils. During the first days after the operation all conditioned reflexes disappeared; then they reappeared, disappearing only during the convulsive attacks.

The right vertebral artery was tied and cut in the neck fifteen days after the third operation. The fourth operation did not produce any particular changes in the general behavior of the animal or in the state of the conditioned reflexes. The dog was killed thirty-nine days after this operation. During this last period of investigation the attacks became rarer and the magnitude of the conditioned reflexes was increased. The discrimination of the negative stimulus of beating of a metronome at a rate of 60 from the positive stimulus at a rate of 120 was reestablished. The drowsy condition during the experiments was permanent, continuing to the end of the investigation.

TABLE 12.—*Experimental Extinction of Conditioned Reflexes under Normal Conditions and After Ligation of the Arteries Supplying the Brain*

Animal	Conditioned Stimulus*	Conditioned Reaction	Number of Applications Necessary for Complete Extinction of the Effect of Positive Stimulus				
			Before Operation (Normal)	After First Operation	After Second Operation	After Third Operation	After Fourth Operation
Dog 4.....	Tone (1,000 c.p.s.)	Salivary	..	6	4	3	3
Dog 8.....	Electric bell.....	Motor	14	14	5	4	..
Dog 24.....	Electric bell.....	Motor	19	10	3	..	..
Dog 23.....	Tone (1,000 c.p.s.)	Salivary	6	6	4	3	..

* The stimulus was given repeatedly, at three minute intervals, without réenforcement by food, until the conditioned salivary or motor reactions had completely disappeared at two successive trials.

With this dog, as with the previous dogs, experiments for the extinction of the reflex to a tone of 1,000 cycles per second were carried out. The results of these experiments are shown in table 12. In dog 23, as may be seen, under normal conditions six trials of the positive stimulus without reenforcement were necessary before complete disappearance of the conditioned reflex was obtained. After the first operation the number remained the same, but after the second operation only four trials and after the third only three trials were necessary for complete extinction. This shows the increase in the strength of the process of inhibition. On comparing these data with experimental extinction in the other dogs (table 12) it is seen that the number of trials before extinction was obtained diminishes proportionately with the increase in number of tied arteries.

COMMENT

Ligation of the arteries supplying the brain in dogs brings about disturbances of the higher nervous activity which are manifested in changes in the state of the conditioned reflexes both positive and negative. Simultaneous ligation of three arteries, both common carotid and one of the vertebral arteries, produces slight and temporary changes

which can be observed in the first days after the operation. After ligation of three arteries, as in dog 24, fairly strong excitement was observed during the experiment, which was carried out on the fifth day after the operation. This excitement was accompanied by disinhibition of the negative conditioned reflexes. The absolute differentiation of beating of a metronome at a rate of 120 was disinhibited completely. The long delayed conditioned motor reaction to the sound of a buzzer was also disinhibited. The dog had not returned to normal until the thirteenth day after the operation. In the case of dog 23 the first experiment after the ligation of three arteries was carried out on the ninth day. On this and the following few days excitement and disinhibition of differentiations were observed.

Simultaneous ligation of four arteries, both common carotid and both vertebral arteries, always produced symptoms of disturbance of cortical activity. Dog 4 survived this operation at the age of 1½ months. The dog was investigated by the method of conditioned reflexes during nineteen months. The changes in the general behavior of this dog after ligation of the arteries are characteristic of a so-called weak, easily inhibited type of nervous system. The increased inhibition was especially pronounced during the application of the negative (inhibitory) stimuli. As a rule, after negative stimuli there developed a strong after-effect inhibition and drowsiness, passing into sleep. The solution of difficult problems was not within the capacity of this type of animal. Even a very slight intensification of the inhibitory process, or a conflict of the nervous processes (a quick change from excitement to inhibition, or vice versa), produced complete destruction of conditioned reflexes, and the animal fell into a hypnotic state. A still greater restriction of the cerebral circulation produces temporary disappearance of the conditioned reflexes, disinhibition of differentiations and increase of the inhibitory process. An even more pronounced disturbance was observed in the acoustic analyzer; the highest limit of hearing was reduced and there was no longer any discrimination of the negative auditory stimuli (tones of 25,000 and 300 cycles per second) from the positive stimuli (tones of 18,000 and 100 cycles per second).

Simultaneous ligation of the subclavian and common carotid arteries and the costocervical and omocervical trunks on one side was performed in dog 8 at the age of 2½ months. This operation did not produce any noticeable disturbances in the higher nervous activity. After the first operation dog 8 was observed by the method of conditioned reflexes during seventeen months. The general behavior of the dog and the state of the positive and negative conditioned reflexes were normal.

The most pronounced disturbances of the higher nervous activity after ligation of the arteries were observed in dog 23. This dog was operated on at the age of about 4 years. The intervals between opera-

tions were comparatively short, and ligation was performed simultaneously on the two sides. In consequence, in dog 4 conditions were less favorable for the development of collateral passages and anastomosis.

It must be remarked that with all the dogs simultaneous ligation of both vertebral arteries at the back of the neck between the first and the second cervical vertebra produced more pronounced symptoms of disturbed cortical activity than simultaneous ligation of, for instance, both internal carotid and both occipital arteries. Unfortunately, I am not able to say, on the basis of my observations, how long these disturbances continue after ligation. Acute disturbances disappear during from ten to twelve days after operation. This period is sufficient for the development of collateral passages. These disturbances were not the result of the operative trauma, since the postoperative period passed without any complications whatever. After ligation of the arteries supplying the brain there remained, however, permanent symptoms which indicate, to a greater or lesser degree, abnormality of the activity of the cortex.

CONCLUSIONS

1. Simultaneous ligation of four arteries (both common carotid and both vertebral) in dogs produces functional disturbances of higher nervous activity. These disturbances may be either temporary or permanent and may also vary in character and intensity.

2. The temporary disturbances are most pronounced during the first ten to twelve days after operation and are manifested in the complete disappearance of the conditioned reflexes. After the restoration of the conditioned reflexes, disinhibition of the responses to negative conditioned (inhibitory) stimuli is observed.

3. The elementary functions of the cortex, as manifested in the establishment of conditioned reflexes and the formation of simple differentiations, may be completely restored.

4. The more delicate functions of the cortex, as represented by the establishment of fine discriminations and the formation of long delayed conditioned reflexes, may be eliminated either permanently or for a long time.

5. After ligation of the arteries supplying the brain both fundamental nervous processes, excitation and inhibition, are weakened; when the general excitability is decreased, inhibition dominates.

OTOLOGIC FINDINGS IN OCULOGYRIC CRISES

A CONTRIBUTION TO THE STUDY OF THE SUPRAVESTIBULAR PATHWAYS

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In 1921 [1] the oculogyric crisis in chronic encephalitis was described as a paroxysmal, intermittent deviation of both eyeballs, usually upward or upward and to one side, accompanied by a deviation or tendency to deviation in the same direction on the part of the head. The spasms as a rule lasted several hours, were generally painful and were often accompanied by signs of excitement and other abnormal psychic states.

Since then this condition has been reported many times, but writers are by no means agreed as to the nature of the paroxysms. Some believe them to be functional, and others—and they appear to be in the majority—consider them to be organic manifestations of encephalic lesions with the emotional phases as secondary accompaniments. The implications of the problem for the oculist and otologist lie in their obvious bearing on the complex and much disputed mechanism of associated ocular movements and particularly in the relationship of the vestibular apparatus to these movements.

My interest in this curious symptom began with a case which was referred by the ophthalmologic department of the Research and Educational Hospital for labyrinthine tests.

REPORT OF CASES

CASE 1.—*History.*—A man aged 23 stated that about three years prior to admission to the hospital he began to have attacks in which the eyes would suddenly turn up and remain so for about half an hour. This happened sometimes two or three times a day and at other times at intervals of several days; during the attack he was completely unable to bring the eyes down. The patient dated the condition from a blow which he received over the right eye some time prior to the onset of the paroxysms. There was no unconsciousness at the time, but shortly afterward he noticed that he could not see well with the right eye. He had ptosis of the right upper lid, which had been present prior to the accident, and a speech difficulty which began at about the same time as the ocular spasms.

Ophthalmologic Findings.—There were an old choroidal tear close to the macula of the right eye, deficient vision in this eye and moderate ptosis of the upper lid; there were no abnormalities in the left eye.

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1. Oeckinghaus, W.: Encephalitis epidemica und Wilsonische Krankheit, Deutsche Ztschr. f. Nervenh. **72**:294, 1921.

Otorhinologic Examination.—No abnormalities were found except some evidence of a possible persistent nasopharyngeal duct and moderate chronic laryngitis. There was slight retraction of the tympanic membranes. Tests with the voice and with the tuning fork showed good hearing with some increase of bone conduction and slight elevation of the limit for low tones on both sides.

Vestibular Examination.—There were nystagmoid movements when the patient looked up and a definite horizontal nystagmus of 1 degree to the right when the head was put 60 degrees back. There was no spontaneous past pointing, Romberg sign or disturbance of gait when the eyes were closed. The results of rotation tests were as follows: With the head 30 degrees forward rotation to the right (ten times in ten seconds) produced horizontal nystagmus to the left lasting thirty-three seconds, slight past pointing to the right with both hands and vertigo to the left. Rotation to the left (ten times in ten seconds) produced horizontal nystagmus to the right lasting thirty seconds, slight past pointing to the left with both hands and vertigo to the left. The last finding was checked on two other occasions, with the same result. With the head 120 degrees forward rotation to either side failed to elicit any falling when the patient sat up.

Rotation to the right with the head over the right shoulder (ten turns) caused nystagmus of 2 degrees downward for eighteen seconds. Rotation to the left with the head over the right shoulder caused nystagmus of 2 degrees upward for twelve seconds. Rotation to the right with the head over the left shoulder caused nystagmus of 2 degrees upward for sixteen seconds. Rotation to the left with the head over the left shoulder caused nystagmus of 2 degrees downward for seventeen seconds.

Caloric reactions, tested with the Bárány douche, with the water at 68 F., were: Right ear—in forty-two seconds, horizontal rotatory nystagmus of 2 degrees to the left for one hundred and fifteen seconds; with the head back, horizontal nystagmus to the left for three minutes, ten seconds. Falling and past pointing were slight, but correct. Left ear—in fifty-five seconds, horizontal rotatory nystagmus of 2 degrees to the right for one hundred and twenty-five seconds; with the head back, horizontal nystagmus to the right for eighty-three seconds. Falling and past pointing were slight, but correct.

A feature noted during the vestibular tests was the complete insusceptibility to stimulation (absence of nausea, pallor or sweating), no matter how prolonged the stimulation. Optic nystagmus, tested with an apparatus devised for the purpose, could be induced normally in all the cardinal directions.

Observations During a Crisis: The eyeballs were drawn upward and to the right; a few minutes later, upward and to the left. While the eyeballs were in the latter position there was a rapid oscillatory nystagmus upward and to the left in the right eyeball and downward and to the left in the left eyeball. The head was drawn back, and the patient complained of pain in the frontal region. A syringeful (100 cc.) of very cold water (from 10 to 15 C.) introduced into each ear was ineffective in the production of typical caloric nystagmus. During another attack observed in my office several months later essentially the same features were noted. At this time the caloric test with the Bárány douche (68 F.) gave negative results for caloric nystagmus, but the Romberg test showed vestibular falling in the proper direction. The rotation test was then performed with the head over one shoulder so as to produce nystagmus downward. Rotation to the right with the head over the right shoulder was unsuccessful, but rotation to the left with the head over the left shoulder produced a good nystagmus downward and abolished the crisis, i. e., caused the eyes to return to their normal position and brought back the power of voluntary movement, and the state persisted for the rest of the afternoon.

Clinical Summary.—There were an old injury of one eye, evidence of chronic parkinsonism and cephalo-oculogyric crises. The otologic findings indicated good hearing in both ears. Between attacks vestibular function was normal with regard to nystagmus, past pointing and vestibular falling after the caloric test, but abnormal with regard to the direction of vertigo following rotation to the left, with falling after rotation with the head 120 degrees forward, and susceptibility following prolonged stimulation. During the attack there was dissociated nystagmus suggesting a central origin. There was evidence that the caloric test produced a vestibular reaction to falling following irrigation but no nystagmus, while rotation with the head over the left shoulder not only produced a typical nystagmus downward but cut short the attack.

I have had the opportunity to examine at my office five other patients who exhibited oculogyric crises and shall briefly state the significant findings in each case.

Case 2.—The patient and the patient in case 3 were referred by Dr. Krumholz with a diagnosis of postencephalitic parkinsonism. Five years after an attack of epidemic encephalitis this man began to have sudden, intermittent deviations of the eyes and head, generally upward, sometimes downward. Ocular examination indicated weakness of the muscles of convergence (18 cm. near the point of convergence) and accommodation for his age (tested with the Duane rule) and jerkiness of the voluntary movements of the eye (*sakkadierte Augenbewegungen*). No other ocular findings indicating an abnormality were noted. The cochlear function was normal.

Vestibular examination did not reveal spontaneous vertigo, nystagmus, past pointing or falling. Horizontal and horizontal-rotatory nystagmus following rotation and the Bárány douche were normal; vertical nystagmus induced by rotating the patient with the head over the shoulder so as to induce it in a downward direction was somewhat prolonged, but upward nystagmus could be produced only for one or two beats, after which the direction changed to horizontal.

Vertigo following rotation was found to be diminished slightly but in the proper direction; past pointing, on the other hand, was persistently in the wrong direction after rotation to the right. Following the caloric test there was failure to past point. Galvanic tests gave normal results. Marked lack of susceptibility to all forms of vestibular stimulation was noted.

I had no opportunity to observe an attack in this patient but append a photograph taken during a crisis, which was furnished by Dr. Krumholz and will serve to illustrate a typical spasm (fig. 1).

Case 3.—In the patient the ocular findings were limited to weakness of convergence and jerky movements of the eyes. Cochlear and vestibular examination gave normal results except that vertigo was absent and susceptibility to stimulation was markedly diminished. Observation of an attack revealed horizontal conjugate deviation of the head and eyes to the right, which the patient was able to overcome momentarily. I could not produce nystagmus in the opposite direction with 100 cc. of water at from 10 to 15 C. but was able to do so with the Bárány douche.

Case 4.—The patient was referred with a diagnosis of chronic postencephalitic parkinsonism by Dr. Alfred P. Solomon. Ocular examination gave negative results except for moderate weakness of the muscles of convergence and accommodation. Cochlear function was normal. There were no spontaneous vestibular manifestations. In the rotation test with the patient's head over her shoulder it was noted that nystagmus upward could be produced only for eight seconds, while nystagmus downward was produced for eighteen seconds. The other tests for nystagmus, past pointing, falling and vertigo gave a normal reaction to rota-

tion and caloric and galvanic stimuli. It was noted that susceptibility to stimulation was slight. In a crisis which I witnessed in this patient (a young married woman) the eyeballs and head were seen to be drawn directly upward; there was rapid rotatory nystagmus to the left interspersed with vertical nystagmus upward. She could bring her eyes down momentarily, but they would go up again in a series of clonic movements. Rotation of the patient with her head over her shoulder failed to produce nystagmus opposite to the direction of the deviation. The caloric test with 100 cc. of water at from 10 to 15 C. failed to produce horizontal nystagmus while the eyes were drawn up, but when the patient voluntarily brought them down to the midline good horizontal rotatory nystagmus in the proper direction was seen.

CASE 5.—A young man, referred by Dr. James Lebensohn, complained that his eyeballs would suddenly turn upward while he was reading or playing cards

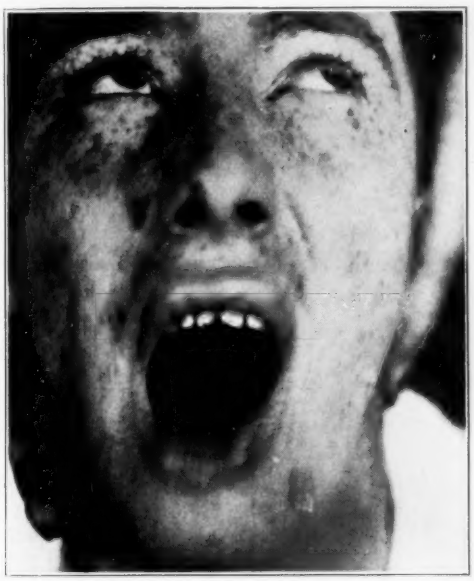

Fig. 1 (case 2).—Oculogyric crisis with both eyes and the head drawn back, with the former obliquely upward. This is the most common direction of deviation.

and would continue to turn upward until he went to sleep. The only other complaint was that he slept for abnormally long periods and had great difficulty in waking of his own accord.

Ocular examination gave negative results except for jerkiness of the eyeballs on voluntary movement. Tests of the function of the eighth nerve gave normal results save for complete insusceptibility to vestibular stimulation. A mild attack was witnessed in which the eyeballs were drawn up, but the patient could bring them back to midline by an effort.

CASE 6.—A young woman with oculogyric crises and parkinsonian symptoms, referred by Dr. George B. Hassin, gave a history of sleeping sickness seven years before. Ocular examination gave negative results except for the cog-wheel type of voluntary movement noted in other patients and a moderate degree of alternating strabismus which had been present since childhood. Hearing and vestibular function were normal except for diminished susceptibility to stimu-

lation. Observation of the patient during a paroxysm showed the eyeballs to be up and somewhat to the left, with a rapid oscillatory nystagmus to the left. Irrigation of the left ear with 100 cc. of water at approximately 10 C. stopped this nystagmus for a few moments and produced slight vertigo and past pointing. Rotation to the right produced past pointing, nausea and vomiting; a few minutes later the oculogyric crisis abated and the eyes returned to their normal position. The patient stated that this had never happened before unless she went to sleep.

SUMMARY OF FINDINGS IN THE SIX CASES

Six patients, four men and two women ranging in age from 21 to 39 years, suffering from cephalo-oculogyric crises, were examined for findings relative to involvement of the ocular and cochleovestibular apparatus. Four had tremors, rigidity and other evidence of parkinsonism; two presented no striking neurologic symptoms but were nevertheless considered by neurologists to have a probable postencephalitic state.

Weakness of the muscles of convergence and accommodation or jerky voluntary movements of the eyes were present in five. Cochlear function was good in all. With the exception of one instance (horizontal nystagmus of 1 degree), no spontaneous vestibular abnormality was present. Vestibular stimulation revealed absence of, or diminished, susceptibility in all the patients, perverted or absent vertigo in two, perverted past pointing in one, absence of falling (*Fall-Reaktion*) in one, who also showed perverted vertigo, and absence or impairment of nystagmus downward as induced by rotation with the head over the shoulder in two. Optic (railroad) nystagmus in all cardinal directions could be induced in the intervals between attacks in all the patients. Five attacks were witnessed; in four there was upward or oblique deviation of the head and eyes and in one, horizontal deviation. The ability to induce vestibular nystagmus while the patient was in a crisis was apparently proportional to the strength of the stimulus applied and the severity of the spasm.

OCULOVESTIBULAR FINDINGS REPORTED IN THE LITERATURE

The literature contains many reports of oculogyric crises, but in comparatively few of the cases have careful vestibular studies been made. The eyes have been examined more frequently; they uniformly failed to show evidence of pathologic change in the structure of the eyeball, fundus or visual tract, but jerky movements of the eyes, weakness of the muscles of accommodation and weakness or spasm of the muscles of convergence have been observed frequently.[2] These ocular

2. Teulières, M., and Beauvieux, J.: Les manifestations oculaires tardives dans l'encéphalite épidémique, Rev. d'oto-neuro-opht. **9**:349, 1931. Sauer, L.: Kombination von Akkommodations- und Konvergenzstörung nach Encephalitis, Ztschr. f. Augenh. **71**:140, 1930.

findings are often present in postencephalic states in which oculogyric crises do not occur. The otologic findings may be summarized as follows:

Cochlear function is uniformly good. Spontaneous phenomena are uncommon in relation to the number of patients examined. Helsmoortel and van Bogaert [3] noted vertigo twice and spontaneous nystagmus once in ten cases of oculogyric crises. B. Fischer [4] stated that slight vertical spontaneous nystagmus (presumably of 1 degree) was present in all five of his patients. Vertigo and susceptibility were not present following caloric and rotation tests, and the caloric nystagmus was normal in all; vertical nystagmus downward could not be induced by rotation in two instances. These findings have a general resemblance to those in my cases and to those presented by the patients examined by Stengel.[5]

Hypo-irritability in some cases and hyperirritability in others in response to the Kobrak caloric test were noted by Helsmoortel and van Bogaert; neither of these conditions, however, appears to have been pronounced. During the attack spontaneous nystagmus, chiefly vertical, and difficulty in eliciting the vestibulo-ocular reflex opposite to the direction of the deviation when this had a horizontal component were noted.[6]

THEORIES OF ORIGIN OF OCULOGYRIC CRISES

Although it is my purpose mainly to discuss the relationship of oculogyric crises to the vestibular apparatus, it is essential if a proper perspective is to be preserved that other leading views regarding their origin be presented. Epidemic encephalitis, which is the primary disease in these cases, may attack practically any part of the central nervous system, but it shows a marked predilection for the midbrain and brain stem and particularly for the extrapyramidal system; corresponding to this predilection the symptomatology in the postencephalitic state, while protean, is dominated by parkinsonian signs combined with hypokinesis or hyperkinesis consisting of rhythmic tremors, myoclonia and other involuntary movements. Various signs of nuclear ocular involvement as well as abnormal vestibular findings are common in both the acute and the chronic stage of epidemic encephalitis. While the symptoms

3. Helsmoortel, J., and van Bogaert, L.: Recherches sur l'état des fonctions vestibulaires dans les crises oculogyres de l'encéphalite (10 cas), J. de neurol. et de psychiat. **27**:574, 1927.

4. Fischer, B.: Ueber vestibulare Beeinflussung der Augenmuskulatur bei der Encephalitis epidemica, Deutsche Ztschr. f. Nervenh. **81**:164, 1924.

5. Stengel, E.: Weitere Beiträge zur Kenntnis des post-encephalitischen Blickkrampfes, Ztschr. f. d. ges. Neurol. u. Psychiat. **127**:441, 1930.

6. Marinesco, M. D., and Draganesco, S.: Nouvelles recherches sur l'état des reflexes vestibulaires chez les parkinsoniens post-encéphalitiques ayant des crises de déviation conjugée des globes oculaires seule ou associée à une déviation de la tête, Rev. d'oto-neuro-opht. **6**:50, 1928. Helsmoortel and Bogaert.[3]

mentioned form a large percentage of the sequelae, the disseminated character of the lesions in many cases is such that almost any nervous disorder may be produced or simulated by this disease. Oculogyric crises may be present in patients exhibiting many other signs of postencephalitic disease or may be practically the sole finding; while the spasms are sometimes grouped together with other involuntary movements noted in patients with this condition even a cursory examination reveals striking differences between them and other so-called hyperkinetic phenomena—a fact which probably accounts for the interest aroused in the crises and the variety of explanations offered in their behalf.

Theory That the Crises Are Hysteriform.—Some observers[7] have endeavored to identify oculogyric crises with hysterical phenomena, such as paralysis or contractures. While there is a superficial resemblance in some respects, such as the occasional power of suggestion or emotion to bring on an attack, most authors unite in rejecting this explanation as incompatible with the definite organic changes in the brains of patients who have had epidemic encephalitis. The case against this hypothesis from a clinical standpoint was stated by Hall.[8] 1. The description of the attacks indicates that the main features are essentially similar in widely separated countries instead of taking on varying characteristics as would be expected in simulation. 2. Oculogyric crises do not arise by imitation. 3. Attacks may be cut short by suggestion, but this has no permanent curative value. 4. The movements are not of a character that can be made voluntarily, which is contrary to the rule in hysteria. Hall referred specifically to the fact that in a voluntary movement of the eyes upward there is associated wrinkling of the frontalis muscle, which is lacking in cases of oculogyric crises in which the deviation is wholly or partly vertical (a fact noted in my cases). To this may be added the presence of peculiar forms of nystagmus during the attacks as exemplified in some of the patients whom I examined.

Hall put forward the idea that the ocular deviations are due to inhibition rather than to spasms of groups of muscles and associated them with abnormal states of the "sleep center," which is supposedly located in the vicinity of the fourth ventricle and may be affected in the postencephalitic state as well as during the acute stage of the disease. He endeavored to demonstrate that the ocular deviation during sleep is not always upward, as is generally considered, but may be lateral as well. No explanation, however, was offered for the changes in direction

7. van Bogaert, L., and Delbeke: Contagion des crises oculogyres chez des parkinsoniens postencéphalitiques, J. de neurol. et de psychiat. **26**:269, 1926.

8. Hall, A. J.: Schorstein Memorial Lecture on Chronic Epidemic Encephalitis with Special Reference to the Ocular Attacks, Brit. M. J. **2**:833, 1931.

which frequently take place even in the same attack, the concomitant nystagmus and deviation of the head and the difficulty in producing nystagmus opposite to the deviation by means of labyrinthine stimulation.

Theory That the Crises Result from Release of Cortical Inhibition.—McCowan and Cook,[9] Wimmer [10] and others have identified oculogyric crises with other phenomena of a hypokinetic nature occurring in patients with chronic encephalitis, such as various athetoid and myoclonic movements, motor tics and general convulsions. They put forth the theory that the lesions responsible for the crises lie not in the lower centers for conjugate deviation (i. e., in the midbrain or brain stem) but in the association paths leading to them from the cortex. They considered that as a result of these lesions there is in patients exhibiting these phenomena a diminution of the normal cortical inhibition over motor acts, thus making possible the ocular spasms which are comparable to other manifestations of a "release" nature. Kinnier-Wilson [11] and others have pointed out the unsoundness of the assumption of a common origin for all the various involuntary movements in chronic encephalitis and kindred diseases; at this time it is necessary only to point out the intermittent character of oculogyric crises as contrasted with the more or less constant presence of most of the other involuntary movements included in this group, the tonic character of the spasm as against the clonic nature of some of the other manifestations and the distinctly postural pattern of cephalo-oculogyric crises as compared with the irregularity and aimlessness of athetosis and myoclonia. Furthermore, the results of some recently reported postmortem studies of the brains of patients who suffered from oculogyric crises, while not conclusive in solving the problem, indicate definitely that cerebrocortical lesions are either slight or absent.

Jeliffe,[12] who has made an exhaustive study of the emotional and psychic manifestations accompanying oculogyric crises, visualized them as a compulsion phenomenon on an organic substratum in the cortical pathways. This theory is open to some of the same objections as the one just mentioned, as well as to some of those raised by Hall, which were previously stated.

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9. McCowan, P. K., and Cook, L. C.: The Ocular Syndrome of Epidemic Encephalitis, in Lord, J. R.: Contributions to Psychiatry, Neurology and Sociology, dedicated to the late Sir Frederic Mott, New York, Paul B. Hoeber, Inc., 1929.

10. Wimmer, A.: Tonic Eye Fits, Acta psychiat. et neurol. **1**:173, 1926.

11. Wilson, S. A. K.: Modern Problems in Neurology, New York, William Wood & Company, 1929.

12. Jelliffe, S. E.: Psychopathology of Forced Movements in Oculogyric Crises, Washington, D. C., Nervous and Mental Disease Publishing Company, 1932.

Theory That the Crises Are Epileptoid.—This has been advanced by some (Sterling;[13] Senise[14]) on the presumption of meningeal irritation in the vicinity of the second frontal convolution adjacent to the supposed center for ocular movements. The objections to this view are that the conjugate deviations due to cortical irritation as seen in man are practically always horizontal, while those which occur during oculogyric crises are generally vertical or oblique; that oculogyric crises can be brought on at times by various emotional factors or by suggestion, which is not the case with epileptoid seizures, and that the eyes can often be returned momentarily to the midline or the direction of the deviation may change during the attack, which is not true of epileptoid seizures. Finally, as has been stated, postmortem evidence is decidedly against any theory of cortical or meningeal origin as an explanation of oculogyric crises.

Theory That the Crises Are Due to Lesions in the Vicinity of the Corpora Quadrigemina.—This view has been proposed on the theory that the nuclei mentioned form a station for voluntary vertical movements and that consequently spasms would be due to an irritation in this vicinity.[15] The evidence that the corpora quadrigemina fulfil any such function rests on feeble ground, as was pointed out by Spiller[16] in his admirable review of corticonuclear pathways. The theory furthermore takes no account of the accompanying deviation of the head, the intermittent character of the spasm and the manifest influence of fatigue, suggestion and emotional states in initiating the attack. The ability of the patient to perform voluntary ocular movements in all directions during the intervals—a finding noted in nearly all the recorded cases—also tends to weaken this hypothesis, as it is difficult to conceive of a process which would indefinitely manifest itself as an irritation without at some period manifesting paresis or paralysis of voluntary associated ocular movements.

RELATIONSHIP OF THE VESTIBULAR APPARATUS TO OCULOGYRIC CRISES

Many observers have commented on the frequency of vestibular involvement in cases of epidemic encephalitis as evidenced by vertigo, nystagmus and disturbances of equilibrium. Stern[17] has stated his belief that the vestibular nerve is more commonly injured than any

13. Sterling, W.: Le type spasmodique tétanoide et tétaniforme de l'encéphalite épidémique; remarques sur l'épilepsie extra-pyramidale, Rev. neurol. **2**:484, 1924.

14. Senise, T.: Su la genesi a la natura delle crisi oculogire nei post-encefalitici, Riv. di pat. nerv. **35**:69, 1930.

15. Bing, R., and Schwartz, L.: Les crises oculogyres verticales du parkinsonisme post-encéphalitique, Encéphale **20**:150, 1925.

16. Spiller, W. G.: Corticonuclear Tracts for Associated Ocular Movements, Arch. Neurol. & Psychiat. **28**:251 (Aug.) 1932.

17. Stern, F.: Die epidemische Encephalitis, Berlin, Julius Springer, 1928.

other; Barré and Reys,[18] Poston [19] and others have professed to distinguish a special labyrinthine form of this malady. In view of these facts as well as because of the common predilection previously mentioned, it is not surprising to find frequent indications of abnormal labyrinthine function in persons in a postencephalitic state. While no uniform symptom complex exists, the most characteristic findings have been summarized by Portmann [20] as dissociation between the results of the rotation and those of the caloric tests with a tendency to hypofunction as indicated by the reaction to the latter test and lack of susceptibility to stimulation. There is seldom any evidence of cochlear pathologic change, and in general the evidence points to a central vestibular lesion.

Are there any otologic findings peculiar to oculogyric crises as distinguished from other postencephalitic states? In two of my cases I was unable to elicit a proper vertical nystagmus downward—a sign which has also been noted by other observers; this may be of significance, although it is not present in all cases in which vertical deviations occur during the crises. Some of the other findings—the anomalies of past pointing (particularly in the presence of normal vertigo) and the perversion or absence of vertigo—are interesting, but under the circumstances they cannot be said to have any specific value, as they are a common finding in patients in a postencephalitic state who show no ocular spasms. In general I must subscribe to the conclusions of Helsmoortel and van Bogaert [3] in this respect, namely, that there is no constant or uniform group of vestibular findings which are characteristic of oculogyric crises. Some authors [21] have considered the spasm itself to be the result of an abnormal labyrinthine excitation, basing the idea on the fact that vestibular tests designed to produce nystagmus opposite to the deviation (when this shows a horizontal as well as a vertical component, which is commonly the case) are as as a rule slightly or not all effective, while tests which produce nystagmus in the direction of the deviation cause prolonged responses. My examination revealed marked differences in the effect of vestibular stimulation during the crisis in different patients and considerable differences in the result (as to overcoming the deviation and producing nystagmus in the opposite direction), depending on whether the caloric or the rotation test was used, as well as in the length of the caloric stimulus; galvanic stimulation [22]

18. Barré, J., and Reys, L.: L'encéphalite épidémique à Strasbourg: Sa forme labyrinthique, Bull. méd., Paris **35**:256, 1921.

19. Poston, R. I.: Vestibular or Labyrinthine Epidemic Encephalitis, Brain **49**:482, 1926.

20. Portmann, G.: Les manifestations cochléo-vestibulaires tardives de l'encéphalite épidémique, Rev. d'oto-neuro-opht. **9**:241, 1931.

21. Fischer,[4] Marinesco and Draganesco.[6]

22. Reys, L.: Sur une variété spéciale de troubles des mouvements associés des yeux, Rev. d'oto-neuro-opht. **3**:65, 1925.

was probably the most effective in this respect. That hyperexcitability of the vestibular centers exists on one side was not evidenced by either the Romberg test after caloric stimulus (past pointing tests are not feasible, owing to the deviation of the head) or by subjective complaints on the part of the patient following vestibular stimulation applied during the crisis; neither of these criteria gave any evidence of imbalance between the labyrinthine areas.

Careful consideration of the vestibular findings in the patients I examined as well as in the reports of others does not support the theory of a lesion in the inner ear, the vestibular nerve or the vestibular nuclei in the brain stem as the causative factor of oculogyric crises. Not only is there no case in which lesions of these structures were observed post mortem (in conditions other than encephalitis) in a patient who during life had exhibited these ocular spasms, but present conceptions of vestibular structures below the level of the pons would make it difficult to explain the occurrence of oculogyric crises on such a basis. The facts suggest that any abnormalities of the vestibular apparatus observed in these patients are coincidental rather than a direct cause of the paroxysms.

The Experiments and Theories of Muskens.—Among the earliest known and most striking phenomena which occur following injury of the vestibular pathways in lower vertebrates are forced movements of the eyes, head and body in various planes. A familiar and classic example is furnished by the experiments on pigeons of Flourens and Ewald, in which removal of the horizontal canals gave rise to forced movements of the head and eyes in this plane, while removal of the frontal and sagittal canals caused corresponding movements in those planes. In the rabbit, which has been studied rather thoroughly, the general character of the movements is similar, with the addition of paroxysms of rolling movements or forced deviations of the head.[23]

That similar forced movements occur as the result of injury to the vestibular nuclei and the posterior longitudinal bundle as well as to the labyrinth has been demonstrated by many observers. To Muskens of Amsterdam,[24] however, belongs the credit of having analyzed these

23. Camis, M.: Physiology of the Vestibular Apparatus, translated by R. S. Creed, New York, Oxford University Press, 1930.

24. Muskens, L. J. J.: An Anatomico-Physiological Study of the Posterior Longitudinal Bundle in Its Relation to Forced Movements, Brain **36**:352, 1914; Central Connections of the Vestibular Nuclei with the Corpus Striatum and Their Significance for Ocular Movements and for Locomotion, ibid. **45**:454, 1922; Pathology of Post-Encephalitic Ocular Disturbances in the Light of Recent Anatomical and Physiological Research, J. Neurol. & Psychopath. **8**:132, 1927; Les troubles vestibulaires supranucléaires, Rev. neurol. **50**:155, 1927; On Tracts and Centers Involved in the Upward and Downward Associated Movements of the Eyes After Experiments in Birds, J. Comp. Neurol. **50**:289, 1930.

movements and traced the pathways subserving them not only up to and including the longitudinal bundle but beyond it. He worked with cats by means of lesions inflicted in various parts of the brain and combined his observations with postmortem studies of the resulting degeneration. He was able to demonstrate: first, that the forced movements occur only when the vestibular nuclei, the longitudinal bundle and its terminal nuclei (nucleus of the posterior commissure and nucleus interstitialis) or certain fibers running between the latter and the oral portion of the globus pallidus are injured; second, that the direction of the forced movements was reversed in instances of homolateral lesions beyond the level of the posterior commissure, indicating a decussation of the connection between the commissural nuclei (nucleus of the posterior commissure and nucleus interstitialis) and the pallidum to the opposite side, and third, that by making isolated lesions of the vestibular and commissural nuclei he was able to produce separately movements in the horizontal or frontal planes, corroborating anatomic studies which indicated the existence of separate tracts for movements in different planes running from the individual canals through certain nuclei all the way to the pallidum. He was not able to produce falling backward or forward by injuries of the midbrain, but on the basis of later experiments in birds he concluded that the fibers for these associated movements run from Deiters' nucleus to the cerebellum and return to the midbrain and eventually to the pallidum by way of the superior peduncle.

The similarity of forced movements elicited by his experiments and the forced deviation of the eyes and head witnessed in oculogyric crises led Muskens to the conclusion that the latter, like the former, are the result of injuries to the vestibular apparatus. For various reasons, the chief of which are that the majority of these deviations possess both a vertical and a horizontal component (movement in sagittal and horizontal planes) and that the vertical component is seldom absent, he concluded that the lesion specifically involved the tracts beyond the commissural nuclei running to the pallidum from these nuclei or coming from the superior peduncle. As the majority of the deviations were oblique he postulated the most frequent lesion as being in front of the posterior commissure, where both the tracts which govern sagittal movement, coming from the cerebellum, and those which govern horizontal movement, coming from the posterior longitudinal bundle, would be involved. In summing up Muskens' views as to the origin of oculogyric crises it may therefore be said that like other observers he believed these deviations to be of vestibular origin, but unlike them he placed the lesion not in the vestibular nuclei or the posterior longitudinal bundle but in certain connections between the latter and the pallidum which he termed the third vestibular neuron. The entire

vestibular apparatus, including the pallidal connections, is conceived as governing locomotion in various planes and forced movements in these planes as the result of lesions involving various fibers within this apparatus.

POSTMORTEM OBSERVATIONS IN CASES OF OCULOGYRIC CRISES

A great deal of the speculation relative to the pathogenesis of these deviations has been due to the fact that until recently there was no record of careful study of autopsy material from patients exhibiting this symptom. Ayala [25] mentioned having studied the brain of such

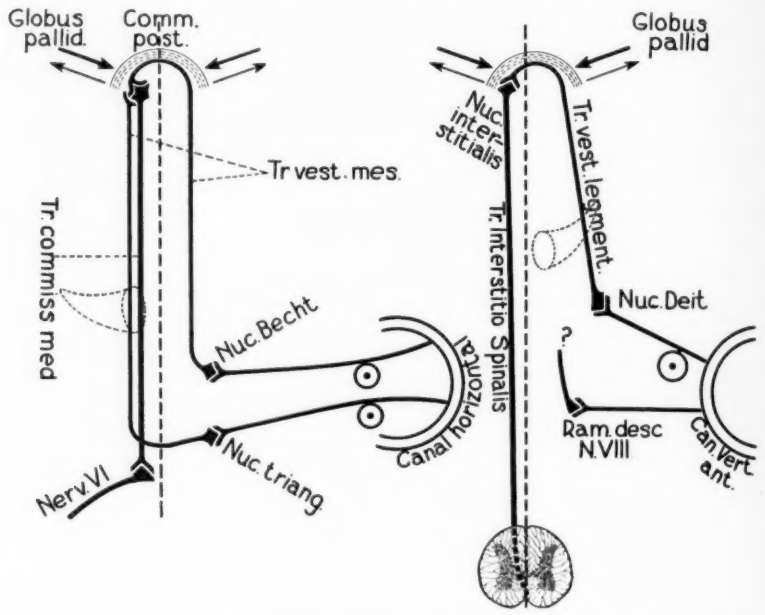

Fig. 2.—Tracts for movements in different planes as constructed on the basis of experimental work by Muskens. On the left are shown the fibers for movements in the lateral plane, originating from the horizontal canal, and on the right, those for movements in the frontal plane, originating from the anterior vertical canal.

a patient, but beyond stating that there were no cortical changes (in refutation of the theory advanced by Senise that the crises are epileptoid) he gave no details. It is evident that even if postmortem studies were arrived at in a number of cases considerable difficulty would be encountered in separating lesions which might account for the oculogyric crises from those responsible for the parkinsonian mani-

25. Ayala, in discussion on Senise.[15]

festations generally present in these patients; in fact, the only studies which would probably carry any weight would be those which dealt with the brain in cases, such as my case 4, in which practically no postencephalitic symptoms were present other than oculogyric crises and narcolepsy. With these considerations in mind I shall review the only two papers on this subject.

The first contribution was that of A. Meyer.[26] His patient showed moderate parkinsonian symptoms and frequent oculogyric crises with movements upward and to the side with accompanying deviation of the head. The result of the autopsy indicated that the nuclei of the corpus striatum, the greater part of the thalamus, the nuclei of the hypothalamus including the body of Luy's, the posterior commissure, the posterior longitudinal bundle and the vestibular nuclei were intact. The only changes of significance were at the level and in front of the posterior commissure (the region designated by Muskens as the meeting place of the tracts for movements in the horizontal and sagittal planes and therefore the probable site of such oculogyric crises as are evidenced in oblique deviations); there were also moderate changes in the terminal nuclei of the posterior longitudinal bundle—the nucleus interstitialis and the nucleus of Darkschewitsch. It appears to me that this report lends support to the theories of Muskens.

The second paper was that of Marinesco and Draganesco.[27] They cited the cases of two patients with chronic postencephalitic parkinsonism accompanied by oculogyric crises with oblique deviations who came to autopsy following death from erysipelas. In these patients the lesions were confined to the midbrain and brain stem but were so diffuse that the authors could reach no conclusions regarding the pathogenesis of the oculogyric crises save that these spasms were not of cortical origin.

SUMMARY OF FACTS AND THEORIES REGARDING THE BASIS OF OCULOGYRIC CRISES

As already indicated, the various theories of nonvestibular origin of oculogyric crises, such as that they are hysteriform, that they result from release of cortical inhibition (due to lesions of association pathways), that they are epileptoid and that they are due to involvement of the corpora quadrigemina, are open to serious objections. The vestibular theory, based on the hypothesis of a causative lesion at the

26. Meyer, A.: Beiträge zur Pathogenese des plötzlichen Hirntodes bei Metencephalitis epidemica zugleich Bemerkungen zur Lokalisation von Blickkrämpfen und Atemstörungen, Arch. f. Psychiat. **89**:25, 1929.

27. Marinesco, G., and Draganesco, S.: Sur la pathogénie des crises oculocéphalogyres chez les parkinsoniens post-encéphalitiques, Rev. d'oto-neuro-opht. **10**:396, 1932.

level of the vestibular nuclei or the posterior longitudinal bundle, is also untenable. Careful consideration of all the facts available, including the results of postmortem studies cited previously, points definitely to the midbrain as the seat of the pathologic changes. It is obvious, however, that none of the usual changes in the basal ganglia and tracts of this region that are commonly found in chronic parkinsonism can be held responsible, as these have been demonstrated many times in patients who during life had no ocular deviations. The views of Muskens, who regarded oculogyric crises as forced movements due to the interruption of pathways connecting the end-stations of the secondary vestibular neurons (terminal nuclei of the posterior longitudinal bundle) to the pallidum, offer an explanation which, while based on experimental evidence, does not run counter to the clinical and anatomic data hitherto available. There are, to be sure, certain differences between the forced movements elicited by Muskens and the others in animals and spasmodic deviations of the head and eyes in patients in the postencephalitic state; these, as will be seen later, can be readily understood in the light of the changing rôle of the vestibular apparatus in man as contrasted with that in animals and do not, by themselves, constitute an argument against the conclusions of Muskens.

POSSIBLE RÔLE OF THE SUPRAVESTIBULAR PATHWAYS IN MAN

The foregoing pages have been devoted to a consideration of a phenomenon which, from a casual point of view, would seem to be of little practical importance. Taken by themselves, oculogyric crises constitute one of the more unusual phenomena which appeared in the wake of recent outbreaks of epidemic encephalitis and which may largely disappear in the course of a generation or two. These paroxysms achieve significance only because of the light they may shed on certain obscure functions of the vestibular apparatus.

The upper portion of the brain stem and the midbrain are the seat of several ganglionic masses with varying yet in some respects similar function. Anatomic evidence shows them to be closely connected with each other and with important sensory and motor centers in the medulla, but the exact nature of this interrelationship is still largely conjectural. It can be stated definitely that nearly all of them are in some way connected with the mechanism of reflex and automatic movements and attitudes. Probably the best known of these centers is the red nucleus, which has been demonstrated through the work of Magnus [28] and Rademaker,[29] particularly the brilliant researches of the latter, to be

28. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

29. Rademaker, G. G. J.: Die Bedeutung des roten Kernes und des übrigen Mittelhirns für Muskeltonus, Körperstellung und Labyrinthreflexe, Berlin, Julius Springer, 1926.

essential to the maintenance of muscle tone and those labyrinthine reflexes which assist the animal to resume a normal attitude when its body or some part of it has been displaced from the normal position. Rademaker's conclusions, which have found wide acceptance, do not appear to me to be in any way antagonistic to the results of Muskens, although there is some controversy between these two authors. The phenomena relating to the labyrinthine righting reflexes which Rademaker abolished by section of the efferent rubrospinal tracts depend on the static portion of the labyrinth as demonstrated by the experiments of Magnus and de Kleijn. The forced movements which result from lesions of the supravestibular pathways have a general similarity to the effects of injuries of the posterior longitudinal bundle, the vestibular nuclei and individual semicircular canals. The attitudes of the eyes and head are also identical with the compensatory movements elicited (*Augendrehreaktion und Kopfdrehreaktion*) in the intact animal by rotation. By analogy, therefore, both as to their origin and as to their similarity to phenomena induced by stimulation of semicircular canals, the forced movements observed by Muskens in his experiments may with great probability be stated to be the result of lesions involving the kinetic portions of the supravestibular connections which are devoted to functions distinct from those under the control of the red nucleus.

The most logical conclusion to be drawn from the experiments of Muskens is, as previously stated, that the phenomena exhibited by his animals were due to loss of tonic stimuli normally transmitted from the various canals as far as the pallidum. There is one apparent objection to this view. It is usually considered that in the end-organ of equilibrium the stimulus to the semicircular canals is movement or angular acceleration, while the static portion (according to some authorities, only the utricle) is concerned with compensatory movements of the eyes, head and limbs as a result of abnormal positions and the maintenance of tone of the skeletal musculature. The latter function involves the constant transmission of tonic influences from the static labyrinth to higher centers, as indicated in the researches of Magnus and Rademaker, so that abnormal attitudes following lesions of the labyrinth or vestibular pathways are likely to be considered the result solely of injuries of this portion of the vestibular apparatus. Indeed, it is commonly stated that the semicircular canals have no tonic effect on the body musculature,[30] and in line with this reasoning the manifest effects of lesions of single canals in animals have been assumed to be effects of irritation. Various facts, however, of which the most significant are the results of nonirritative ablation of the labyrinth with cocaine injected into the middle ear, as carried out in guinea-pigs by

30. McNally, W. J.: Lectures on the Physiology of the Ear, Ann. Otol., Rhin. & Laryng. **39**:248, 1930.

Magnus,[28] made this theory untenable. His conclusions were that the cristae of the canals, like the maculae of the saccule and the utricle, send constant impulses (to the brain), but that the mechanical construction of the canals allows the suppression or increase of these impulses with the consequent production of reflexes of a temporary duration, in contradistinction to those from the otoliths, which may persist indefinitely.

Certain other questions suggest themselves. Both Magnus and Rademaker, working with decerebrate animals, showed that movements of the head and eyes of the character under discussion (*Kopfdrehreaktion und Augendrehreaktion*) as well as nystagmus can be elicited following transection of the brain stem at a much lower level than that of the supravestibular pathways indicated by Muskens. It must be emphasized that their conclusions are valid only under the conditions of the experiments and in no way indicate the mechanism required for the production of these reflexes in the intact animal. For example, the cerebellum has repeatedly been proved to exert a considerable influence on labyrinthine responses, yet Magnus was able to obtain all the vestibular reflexes in animals from which the cerebellum had been entirely removed; alteration of vestibular reflexes due to lesions elsewhere in the brain (above the level of the vestibular nuclei) has also been reported on several occasions. The best explanation of these apparently contradictory facts can be arrived at if one bears in mind that the experiments of Magnus and Rademaker in this respect are simply methods of baring certain vestibular responses in their most primitive form by artificially producing a nervous apparatus (through decerebration or decerebellation) of a very low order. Such experiments, while no doubt of great value in certain respects, offer no indication of the manner in which reflex and automatic activity is brought about in the adult animal possessing a highly developed and fully functioning nervous system. A close study of the literature on the subject leads, on the contrary, to the conclusion that the influence of higher centers on what is commonly regarded as purely vestibular reactions is considerable (for the arguments regarding this question as applied to man the studies of Griffith [31] and other psychologists are revealing).

The demonstration by Muskens of tracts serving movements in various planes running from the labyrinth to the oral part of the pallidum naturally raises the question as to the relationship between these two organs both in animals and in man. With the full knowledge that the functions of the pallidum and its allied ganglia are still considerably in dispute I shall nevertheless devote some consideration to this important point.

31. Griffith, C. R.: An Historical Survey of Vestibular Equilibration, Univ. Illinois Bull. no. 5, 1922.

The pallidum and striatum (nucleus caudatus and putamen) form a group of extrapyramidal nuclei which in mammals is called collectively the corpus striatum. Biologically the pallidum is one of the oldest of the higher centers. In fishes it is regarded as that part of the original cerebral hemisphere through which impressions of smell and taste may bring their influence to bear on the nervous mechanisms regulating movement. With the process of evolution the pallidum is joined by the striatum, which is said to exhibit a structure resembling cerebral cortex as contrasted with the simpler histologic appearance of the pallidum. At the same time definite portions of the midbrain below this level act as centers for the more complicated reflexes subserving posture and locomotion. The anatomic connections and the development of this part of the central nervous system point to the corpus striatum as a station for the coordination of higher automatic activity and the regulation of other nuclei in this region, but support for this view has been difficult to obtain by experimentation on animals, although the work of Lewy [32] and Morgan [33] has furnished some positive results.

The current ideas as to the function of the corpus striatum in man have been elaborated chiefly through the studies of Hunt,[34] C. and O. Vogt,[34] Jakob,[35] Kleist,[34] Foerster,[34] Lotmar,[36] Spatz [37] and others and are based on a considerable accumulation of clinical and postmortem data. These writers differ in some details, but with few exceptions unite in considering this organ as a center for automatic and involuntary movements of various kinds, including associated movements (swinging of the arms in walking, movement of the head back on looking up or to the side on looking to the side) and sudden movements of defense or fright. These automatisms, which depend on the corpus striatum, are principally of the inherited or transmitted type rather than of the acquired variety (e. g., automatic movements as a result of training in sports).[38] Most authors consider the pallidum as the seat of the

32. Lewy, F. H.: Die Lehre vom Tonus und der Bewegung, Berlin, Julius Springer, 1923, p. 527.

33. Morgan, L. O.: The Corpus Striatum, Arch. Neurol. & Psychiat. **18**:495 (Oct.) 1927.

34. Quoted by Lotmar.[36]

35. Jakob, A.: Die extrapyramidalen Erkrankungen, Berlin, Julius Springer, 1923.

36. Lotmar, F.: Die Stammganglien und die extrapyramidal-motorischen Syndrome, Berlin, Julius Springer, 1926.

37. Spatz, H.: Physiologie und Pathologe der Stammganglien, in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927, vol. 10, p. 318.

38. Lyons, L. V., and Brickner, R. M.: Physiologic Differences Between Generic and Individually Acquired Automatic Associated Movements, Arch. Neurol. & Psychiat. **25**:998 (May) 1931.

more primitive movements, with the striatum as the dominant organ. Afferent stimuli originate simultaneously with voluntary impulses originating in the cerebrum (frontothalamic and frontopallidary connections) or are conveyed from the great proprioceptive centers, such as the cerebellum and thalamus, through the striatum to the pallidum, which is the "efferent" portion of the corpus striatum, and thence directly or by way of other extrapyramidal centers to the motor nuclei of the brain stem and spinal cord. The organs sending afferent fibers to the pallidum exert an inhibitory as well as a stimulating influence on the pallidum (*denervatorische und innervatorische*) which is capable of initiating spontaneously various movements of the more primitive type. Marked destruction of the pallidum or its subsidiary centers results in poverty of associated movements, while the removal of inhibitory influence as a result of extensive lesions in the afferent pathways in the superior peduncle (cerebellum), thalamus or striatum results in the "isolation" of the pallidum with the resultant occurrence of involuntary movements of various kinds. A segmental arrangement corresponding to given groups of muscles is assumed by most authors to exist in both the pallidum and the striatum. It must be borne in mind that in clinical practice lesions are seldom limited to a single center or pathway in this region and hence the majority of patients exhibit symptoms due both to partial destruction of the pallidum or subsidiary centers (e. g., the substantia nigra in postencephalitic states) and to lesions of afferent pathways to the pallidum.

As intimated previously, these views of pallidal function and dysfunction rest almost entirely on observation of human material. There is a marked discrepancy between the effects resulting from disease of this and allied ganglia in man and the poverty of symptoms following transection below their level even in higher animals. The latter fact has been used to challenge the conceptions outlined here but the true explanation probably lies in the observation of Spatz that "the lower the scale in the animal kingdom, the less of the extra-pyramidal system is essential for the maintenance of normal muscle tone, body posture and locomotion."

What is the rôle of the supravestibular connections shown by Muskens in these conceptions of the pallidum? From his writings one gathers that Muskens considered the oral portion of the pallidum as a center for locomotion in different planes, which receives its sensory impressions from the different canals in the labyrinth. Presumably this is true only of lower animals, since lesions of this organ in man produce no disturbances of this nature. It is probable that like other afferent fibers they exert a tonic effect on the pallidum and that in their case this influence concerns specifically the movements of the head and eyes in various planes. Possibly they serve as a check on

pallidal movements of this character with a tendency to bring the head and eyes back to the midline. In any event, the occurrence of oculogyric crises is to be viewed as the result of the release of that portion of the pallidum (oral) which is devoted to movements of the head and eyes from the control of one or more of the supravestibular pathways.

An important difference between oculogyric crises in man and the effects of lesions of the supravestibular pathways is worthy of note not only from the standpoint of the explanation offered here but because it indicates to what extent both vestibular and extrapyramidal function in man is modified by higher centers. I refer to the intermittent character of the spasms as contrasted with the more constant effects obtained by Muskens in animals. A close study of the exciting factors in the patients I examined invariably indicated that fatigue, such as reading or playing cards for a long time, excitement, overheating or physical exertion (practically all the patients stated that as a rule the paroxysms occurred at the end of the day) brought on the crises; in some cases prolonged vestibular stimulation was a factor, and in others, as mentioned previously, suggestion could produce a crisis. All these facts can be summed up in one phrase—relaxation of cerebral activity. Evidently as long as the state of the higher centers is at its greatest efficiency normal position of the eyes and head is maintained in spite of abnormal tendencies on the part of the pallidum (it is well known that other types of involuntary movements in extrapyramidal disease may also be suppressed by voluntary efforts), but as soon as this is impaired the latter assumes command until cerebral efficiency is again restored—as a rule by sleep. The site of this psychic activity is probably the frontal lobe, which has been proved by Goldstein [39] to play an important rôle in the maintenance of normal position, coordination and similar acts which one is accustomed to think of as outside the sphere of the cerebrum.

39. Goldstein, K.: Das Grosshirn, in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927, vol. 10.

HORNER'S SYNDROME

A REPORT OF TEN CASES

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The symptom complex known as Horner's syndrome is seen in association with a variety of conditions. It is frequently an important finding in cases of involvement of the nervous system. The syndrome was first described clinically by Horner [1] in 1869, and he recognized that the phenomenon was secondary to paralysis of the nerves of the cervical portion of the sympathetic system. The patient in Horner's case exhibited miosis, partial ptosis, enophthalmos and changes in the vasomotor and sudorific activity of the face. These are the clinical findings usually seen in patients who show the complete syndrome of involvement of the cervical portion of the sympathetic system.

Previous to the publication of Horner's observations experimental work had been done on the autonomic nervous system.[2] In 1727 Petit noted retraction of the eyeball, narrowing of the palpebral fissure and relaxation of the nictitating membrane following section of the "vago-sympathetic" nerve in dogs. His experiments were repeated by others, including Cruikshank in 1795 and Reid in 1839. The first to make a complete study of all the effects resulting from section of the cervical portion of the sympathetic trunk was Claude Bernard,[3] who in 1852 recognized the sequelae previously mentioned and who observed, in addition, that these conditions became reversed if the peripheral end of the cervical portion of the trunk was stimulated. As a consequence the symptom complex herein described is in many places spoken of as the Bernard-Horner syndrome.

Further work on the origin of the autonomic nervous system was done by Budge,[4] who in 1851 found that the sympathetic nerves to

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1. Horner, J. F.: Ueber eine Form von Ptosis, Klin. Monatsbl. f. Augenh. **7**:198, 1869.

2. Fulton, J. F.: Horner and the Syndrome of Paralysis of the Cervical Sympathetic, Arch. Surg. **18**:2025 (April) 1929.

3. Bernard, Claude: Expériences sur les fonctions de la portion céphalique du grand sympathique, Compt. rend. Soc. de biol. **4**:155, 1852. Sur les effets de la section de la portion céphalique du grand sympathique, ibid. **4**:168, 1852.

4. Budge, J. L., and Waller, A.: Action de la partie cervicale du nerf grand sympathique et d'une portion de la moelle épinière sur la dilatation de la pupille, Compt. rend. Acad. d. sc. **33**:370, 1851.

the head arise in the first and second dorsal segments of the spinal cord. Langley [5] identified the levels at which the various types of sympathetic fibers arise, finding that in the cat the fibers which dilate the pupils come predominantly from the first and second dorsal segments, the fibers supplying vasomotor control to the ear and conjunctiva from the third and fourth dorsal segments, and the pilomotor fibers to the face from the fifth and sixth dorsal segments. He also made the significant discovery that the preganglionic fibers to the dilator pupillae muscle terminate in the superior cervical ganglion, where they establish synaptic relations with the postganglionic fibers which pass directly to the pupillary muscles. The more recent work on the central origin of the autonomic nervous system has localized the chief centers in the region of the floor of the third ventricle and in the medulla, which explains why Horner's syndrome can be produced by lesions cephalad to the spinal cord. Horner's original description seemed to correlate his own clinical observations with the physiologic data available at that time, although he made no reference to the experimental work mentioned. Only one known clinical observation of the syndrome was made before the time of Horner; in 1838 Hare [6] described constriction of the pupil and weakness of the levator palpebrae superioris muscle in a patient with a tumor of the neck, but he presumably was not aware of the relationship of the phenomenon to the sympathetic nervous system.

METHOD OF PRODUCTION

It is now known that Horner's syndrome follows injury to, or disease of, the brain stem, the lower part of the cervical or the upper part of the dorsal portion of the spinal cord or its nerve roots, the superior cervical sympathetic ganglion or the postganglionic nerves. Owing to the fact that all the constituent features are not always present and that those which are present vary in the degree of their prominence, there is still some difference of opinion as to the exact etiology of each of the elements of the symptom complex. Higier and Kraus [7] expressed the belief that the motor portion of the syndrome, which consists of ptosis, miosis and enophthalmos, is always present, while the vasomotor, trophic and secretory disturbances are present only with more extensive

5. Langley, J. N.: The Sympathetic and Other Related Systems of Nerves, in Schäfer, E. A. S.: Text-Book of Physiology, Edinburgh, Y. J. Pentland, 1900, vol. 2, p. 616.

6. Fulton, J. F.: Edward Selleck Hare (1812-1838) and the Syndrome of Paralysis of the Cervical Sympathetic, Proc. Roy. Soc. Med. (Sect. Hist. Med.) **23**:24 (Dec.) 1929.

7. Higier, H., and Kraus, W. M.: Vegetative Neurology, Nervous and Mental Disease, Monograph 27, Washington, D. C., Nervous & Mental Disease Publishing Company, 1919, p. 85.

lesions. Miosis; probably the most constant factor, is due to loss of the sympathetic stimuli to the radiating dilator muscle fibers of the iris, with the unopposed parasympathetic stimuli acting on the sphincter pupillae. The pupil reacts weakly to light and in accommodation, but it does not respond to the instillation of cocaine, and the ciliospinal reflex is lost. Ptosis, the next most common finding, is not true palsy of the eyelid due to the involvement of the levator palpebrae superioris muscle but rather pseudoptosis due to loss of sympathetic innervation to the tarsal muscle. The patient is able to raise his eyelid voluntarily. The mechanism of enophthalmos, the third motor symptom, has not been satisfactorily explained. It is considered by most authorities to be due to palsy of the orbital or retrobulbar muscle of Müller. This muscle is believed to be in a state of tonic contraction which disappears with loss of sympathetic function; this allows the globe to sink back into the orbit. Others believe the enophthalmos to be on a trophic basis, associated with a decrease of the orbital fat. There is also some difference of opinion as to whether the retraction of the eyeball is real or apparent, as the narrowing of the palpebral fissure gives the illusion of enophthalmos. Wagener [8] found that enophthalmos could be definitely demonstrated by means of an exophthalmometer in only one of a series of ninety-four cases of Horner's syndrome. He also found that enophthalmos does not immediately follow sympathectomy in man as it does in lower animals, and he expressed the opinion that the orbital muscle has a less definite function to play in human beings.

The remaining constituents of the syndrome of involvement of the cervical portion of the sympathetic system are less constant. Ipsilateral dilatation of the vessels of the head, neck, conjunctiva and upper extremity is seen, and this is, of course, due to paralysis of the sympathetic supply to this region. On the same basis, but occurring less commonly, homolateral anhidrosis is observed. Secondary to these factors, hyperemia and higher temperature of the skin occur in these regions. Horner called attention to this localized hyperemia by means of careful determinations of cutaneous temperature. On occasion, depigmentation of the iris is seen on the involved side. Calhoun,[9] in a study of heterochromia of the irides, found that depigmentation of the iris can occur with paralysis of the sympathetic nerves, but that the palsy is usually congenital or is first noticed in infancy and the difference in the coloring of the irides develops at the time that changes in pigmentation usually occur. Atrophy of one side of the face is considered a

8. Wagener, H. P.: Enophthalmos in Horner's Syndrome, Am. J. Ophth. **17:** 209 (March) 1934.

9. Calhoun, F. P.: Causes of Heterochromia Iridis with Special Reference to Paralysis of the Cervical Sympathetic, Am. J. Ophth. **2:**255 (April) 1919.

possible consequence but is seen with rarity; Cobb and Scarlett [10] observed this to a slight degree in one case, and mentioned an unreported case of Weisenburg's. In Bernard's experimental cases there were also a diminution of intra-ocular tension and progressive diminution in the size of the eyeball; this has been observed clinically on few occasions.

The fact that certain of the constituents of the typical Horner's syndrome occur in some cases and not in others may be due to the area of the nervous system involved. It is now believed that the fibers controlling oculopupillary action arise in the eighth cervical and first dorsal segments of the spinal cord, while the vasomotor, trophic and secretory nerves arise from the second to the sixth dorsal segment. A lesion might involve one set of fibers without affecting the others. Also, in the case of injury to the preganglionic and postganglionic sympathetic nerve fibers, certain fibers may be destroyed while others escape. Cobb and Scarlett [10] found that injuries to the seventh and eighth cervical and first dorsal nerve roots produce the most complete and most severe oculopupillary syndromes, that injuries to the cervical portion of the sympathetic trunk are followed by less severe symptoms and that definite injuries to the spinal cord produce the least pronounced phenomena.

OCCURRENCE

Horner's syndrome has been known to occur in association with various types of injury to, and disease of, the cervical portion of the sympathetic nervous system. The most frequently mentioned etiologic factors are tumor of the spinal cord (case 1) or syringomyelia (case 2) at the level of the ciliospinal center (seventh or eight cervical or first thoracic segment of the spinal cord). Next in order are cervical rib, cervical tumor or enlarged lymph nodes, cervical pachymeningitis (case 3), aortic aneurysm (case 4), mediastinal tumor, disease of the pulmonary apexes (case 5), radiculitis, disease of the esophagus and adenoma of the thyroid gland. The condition frequently follows trauma, especially in the form of bullet or stab wounds. Cobb and Scarlett [10] in 1920 reported eleven cases of Horner's syndrome subsequent to injuries received in war. The symptom complex is invariably seen after operation on the cervical portion of the sympathetic chain, and it is occasionally reported following other surgical procedures, such as thyroidectomy [11] (case 8) or phrenicectomy (cases 9 and 10). Alexander [12]

10. Cobb, Stanley, and Scarlett, H. W.: A Report of Eleven Cases of Cervical Sympathetic Nerve Injury, Causing the Oculopupillary Syndrome, Arch. Neurol. & Psychiat. **3**:636 (June) 1920.

11. Lee, F. H.: Disorders of Motility of the Iris, J. A. M. A. **100**:1395 (May 6) 1933.

12. Alexander, John: The Surgery of Pulmonary Tuberculosis, Philadelphia, Lea & Febiger, 1925, p. 193.

stated that the sympathetic fibers may easily be mistaken for the phrenic nerve and sectioned. A hereditary form of Horner's syndrome associated with atrophy of one side of the face has been described. The condition may occur with involvement of the lower part of the arm or with palsy of the brachial plexus if the lesion is close to the vertebral foramina and the sympathetic rami are injured.[13] Lesions in the brain stem or even in the midbrain or cortex may cause the syndrome. It is seen in cases of disease of the medullary tegmentum, where the oculopupillary center which controls the ciliospinal center is located;[14] it has been described in cases of bulbar palsy with involvement of the medullary sympathetic fibers;[15] it may occur with a lesion at any level of the brain stem or cord which affects the descending supranuclear sympathetic fibers.[16] Owing to the involvement of the carotid sympathetic plexus the condition may be found with tumors of the gasserian ganglion.[17] The syndrome has been reported as occurring with epidemic meningitis, epidemic encephalitis, anterior poliomyelitis and mitral stenosis. The cases of tumor of the upper portion of the pulmonary sulcus, reported first by Pancoast[18] and later by Jacox,[19] are characterized, according to the latter, by "pain, Horner's syndrome, destruction of bone, and atrophy of the hand muscles" (case 5).

REPORT OF CASES

The following ten cases of Horner's syndrome observed in the clinic for neurologic diseases of the University Hospital during the past year illustrate several etiologic factors and give an interesting perspective as to the frequency of the syndrome.

CASE 1.—B. M., a man aged 55, complained of inability to use his legs and of pains through the back and the abdomen. Three years previously he had noticed pain in the left shoulder, and this was followed by atrophy of the interosseus and thenar muscles of the left hand. A year later he noticed pain in the lower portion of the back on the right side, and this gradually descended to the right leg. A year before admission to the hospital the use of the right leg was lost and later the use of the left leg. During the six months before admission to the hospital the patient had noticed frequent spastic contractions of both legs, and there had been complete incontinence of urine and feces.

13. Wechsler, I. S.: A Text-Book of Clinical Neurology, Philadelphia, W. B. Saunders Company, 1928, p. 255.

14. Riley, H. A.: Diseases of the Cerebral Nerves, in Cecil, R. L.: Text-Book of Medicine, Philadelphia, W. B. Saunders Company, 1928, p. 1349.

15. Weschsler, I. S.: A Text-Book of Clinical Neurology, Philadelphia, W. B. Saunders Company, 1928, p. 352.

16. Grinker, R. R.: Neurology, Springfield, Ill., Charles C. Thomas, Publisher, 1934, p. 243.

17. Grinker,[16] p. 546.

18. Pancoast, H. K.: Superior Pulmonary Sulcus Tumor, J. A. M. A. **99:** 1391 (Oct. 22) 1932.

Examination revealed the left pupil to be smaller than the right, but both reacted to light and in accommodation. There was partial ptosis on the left side, but there was no enophthalmos or heterochromia and there were no vasomotor or sudoral changes in the face. There were atrophy of the lumbricalis and interosseus muscles and of the thenar eminence on the left side. The biceps, triceps, knee and achilles tendon reflexes were overactive and equal bilaterally. The abdominal and cremasteric reflexes were not obtained. There were well sustained ankle clonus and a Babinski reflex on each side. Lumbar puncture revealed complete block with xanthochromatic fluid. Roentgenograms of the spine gave no evidence for diagnosis, but on the injection of iodized oil into the lumbar region complete obstruction of the neural canal was found at the level of the second dorsal body. A laminectomy was done on Aug. 2, 1934, by Dr. Edgar A. Kahn, who found a round cell sarcoma rising from the lamina and spinous processes of the seventh cervical vertebra and infiltrating muscle, fascia and bone. There was no appreciable change in the patient's condition following the operation.

CASE 2.—M. E., a girl aged 16, complained of deformity and disability of the left hand which had been progressive during the six weeks previous to her admission to the hospital; the hand was gradually assuming a "claw" position. There had been no pain or anesthesia. There was no history of injury.

Examination showed the left pupil to be smaller than the right, although both reacted to light and in accommodation. There were apparent enophthalmos and slight ptosis on the left side; the left upper eyelid covered more of the iris than did the right, although the lid could be raised voluntarily. On blushing, the left side of the face was more definitely flushed than the right. There was a definite claw hand on the left side, with atrophy of the thenar and hypothenar eminences, and there was some atrophy of the upper and lower parts of the arm, with diminution of the biceps and triceps reflexes. The knee and achilles tendon reflexes were overactive bilaterally, and there were a Babinski reflex and well sustained ankle clonus on the right side, with abortive ankle clonus on the left. Vibratory sensation was lost in the ankles. There were hypesthesia and hypalgesia between the levels of the fourth cervical and eighth dorsal segments. Roentgenograms of the spine were normal, and no spinal subarachnoid block was found. Laminectomy by Dr. Max Peet at the level of the seventh cervical and first dorsal vertebrae revealed an intramedullary cyst. Microscopic examination of the tissue removed for biopsy confirmed the diagnosis of syringomyelia. The patient noticed transient improvement following roentgen therapy, but nine months later drainage of the cyst was required.

CASE 3.—Mrs. J. G., a woman aged 43, complained of difficulty in walking and numbness of the legs, which had been noticed first three years before admission to the hospital; the condition had improved for a time following the use of iodides. A year before admission to the hospital the former symptoms became more marked, and eight months later the patient noticed numbness and weakness of the right hand and paresthesia in the left hand. Shortly after this she began to notice urinary incontinence and increasing constipation. There was no history of pain.

Examination revealed the right pupil to be smaller than the left, but both reacted to light and in accommodation. There was slight drooping of the right upper eyelid, and there was apparent enophthalmos on the right side. The biceps, triceps, knee and achilles tendon reflexes were overactive but equal on the two sides. The Hoffmann sign, the Babinski sign and ankle clonus were present bilaterally. The bladder was distended. There were hypesthesia and hypalgesia to the level of the seventh cervical segment. Vibratory sensation and senses of

motion and position were absent in the left lower extremity and diminished in the right lower extremity. Roentgen examination of the spine gave negative results. Lumbar puncture showed complete spinal subarachnoid block. The spinal fluid was colorless but showed a marked increase of globulin content and 16 lymphocytes per cubic millimeter. Laminectomy by Dr. Max Peet at the level of the sixth and seventh cervical and first dorsal vertebrae revealed a markedly thickened arachnoid which was adherent to and constricted the cord. The constricting and adherent tissue was removed. Microscopic examination confirmed the operative diagnosis of chronic productive leptomeningitis. The postoperative course was slow and protracted, and the patient was discharged six months later with no appreciable change in her condition.

CASE 4.—F. G. M., a man aged 59, complained of pain in the left side of the neck, in the upper part of the thorax and in the region of the shoulder on the left side. He had noticed the onset of pain a year previously, and it had increased in severity during the intervening period. He had also noticed a dry cough and marked loss of weight, and during the few days before admission to the hospital there had been difficulty in swallowing and increasing hoarseness. Thirty-five years previously the patient had a penile lesion which had disappeared under local therapy.

Examination showed the left pupil to be smaller than the right, and there was partial ptosis on the left side. Both pupils were somewhat contracted and reacted sluggishly to light and in accommodation. During the patient's hospitalization the conjunctival vessels on the left side became markedly injected. There was complete fixation of the left vocal cord in the cadaveric position. A tracheal tug was noted, and the trachea was deviated to the right. There was distention of the veins of the left side of the neck and thorax. There was a heaving substernal pulsation with moderate enlargement of the heart. The blood pressure was higher in the right arm than in the left. The tendon reflexes were normal, and the deep and superficial sensations were normal.

A Kahn test of the blood was 4 plus. Examination of the spinal fluid gave negative results. Roentgenograms of the chest showed the presence of a large saccular aneurysm of the aortic arch, with tortuosity of the thoracic aorta. Electrocardiographic studies were considered to be within the range of normal. The patient was given narcotics for the relief of pain and was treated with iodides, bismuth and glyceryl trinitrate. He was discharged feeling somewhat improved, but his physical condition and the Horner syndrome appeared unchanged.

CASE 5.[19]—S. P., a man aged 44, complained of severe pain in the left arm and shoulder of four weeks' duration. The pain radiated down the arm to the inner aspect of the elbow. There was increased warmth of the entire left upper extremity and the left side of the face, with absence of sweating over this area. The pain was accentuated by cold and relieved by heat and narcotics. The patient had palsy of the left side of the face six years before admission to the hospital, but this had improved. There had been an injury to the left eye a few years previously following which there was drooping of the left upper eyelid. The ptosis had increased following the onset of pain.

Examination showed anhidrosis of the left side of the face and neck and the left arm and shoulder, and these areas were warmer than the corresponding areas on the right side. Readings of the temperature of the skin showed a difference of 3 C. between the hands. The left pupil was smaller than the right, there being

19. This case was previously reported by Jacox, H. W.: Superior Pulmonary Sulcus Tumor: Further Observations, J. A. M. A. **103**:84 (July 14) 1934.

a difference of 0.5 mm. in the diameter of the pupils. Both pupils reacted somewhat sluggishly to light and slightly better in accommodation. There was well sustained nystagmus on lateral deviation of the eyes to either side. There was drooping of the left eyelid, with apparent enophthalmos. The left palpebral fissure measured 8 mm. and the right fissure from 11 to 12 mm. Results of readings with the exophthalmometer were from 16.5 to 17 mm. on the right side and from 17.5 to 18 mm. on the left. There was residual palsy on the left side of the face. The biceps, triceps, knee and achilles tendon reflexes were present, somewhat diminished but equal. Vibratory sensation was slightly diminished in the left ankle and markedly diminished in the right ankle. There was a suggestive Romberg sign. There were no cutaneous sensory changes. There was definite clubbing of the fingers. There was a palm-shaped area of blanching over the left scapula. Lumbar puncture and examinations of the spinal fluid gave normal results.

Roentgen examination of the chest showed a soft mass of tissue completely filling the arc of the first rib in the apex of the left lung. There was definite loss of bone substance in the neck and head of the second rib. The diagnosis of tumor in the upper part of the pulmonary sulcus was made. The patient was given deep roentgen therapy with marked relief from pain. Three months later roentgenograms showed a definite decrease in the infiltration of the apex of the left lung, but there was an exacerbation of pain which was relieved by chordotomy.

CASE 6.—Mrs. I. G. J., a woman aged 39, complained of pain in the back of the neck and weakness and disability of the right hand. She had first noticed pain in the right side of the neck and pain and swelling in the right shoulder three months before admission to the hospital. The swelling subsided, but the pain and weakness remained. The patient noticed progressive wasting in the region of the thumb and inability to approximate the thumb and the first finger.

Examination showed the right pupil to be smaller than the left. There was slight drooping of the right upper eyelid, and there was a suggestion of enophthalmos on the right side. The pupils reacted normally, but the reaction was more prompt on the left side. The tendon reflexes were normal. There were no sensory changes. There was definite atrophy of the thenar eminence and of the radial aspect of the wrist on the right side. The fingers were held extended at the metacarpophalangeal joints and flexed at the interphalangeal joints. The patient was unable to approximate the thumb and the index finger of the right hand. Roentgen examination of the cervical portion of the spine revealed slight compression and minimal posterior displacement of the fifth cervical body in relation to the fourth cervical body, which was considered to be the result of an injury. There was hypertrophic arthritis associated with slight narrowing of the intervertebral spaces between the fifth, sixth and seventh cervical vertebrae. The patient did not return to the hospital for further examinations or for treatment.

CASE 7.—B. C., a woman aged 50, complained of pain in the left shoulder and arm, in the left side of the chest and in the region of the left mastoid process. Five years before her admission to the hospital a radical mastectomy had been performed for carcinoma of the left breast, following which the patient noticed some weakness and edema of the left arm but no pain. Nine months before admission to the hospital she first noticed a sensation of pressure in the neck and the gradual progression of the symptoms mentioned. There had been progressive weakness and swelling of the left arm.

Examination showed the patient to be markedly undernourished, with a sallow complexion and a cachectic appearance. The eyes were prominent, the right one more so than the left. The left pupil was small and contracted, reacting just

appreciably to light and in accommodation. The right pupil was medium-sized and reacted normally. The left upper eyelid was ptotic, and it covered the major portion of the iris. There was some dilatation of the conjunctival veins on the left side. On this side the biceps and triceps tendon reflexes were hyperactive, and there was edema of the hand and forearm, with trophic changes in the skin. There were atrophy of the upper arm and hyperesthesia in the distribution of the ulnar nerve. The tendon reflexes and sensation were normal in the lower extremities. There was a well healed mastectomy scar, with no evidence of local recurrence in the region of the scar. The patient refused to have roentgenograms made or to permit a lumbar puncture.

Case 8.—J. C. O., a man aged 47, was first admitted to the hospital with a complaint of weakness, fatigue and loss of weight. Enlargement of the thyroid gland to the right of the midline to the size of a baseball was found, and a right subtotal thyroidectomy was done. Convalescence was uneventful aside from the fact that the patient noticed pain which radiated from the site of the incision to the eye, ear and jaw on the right side. No change was noticed in the pupils, nor was any noted by the surgical staff when he returned to the hospital one month after discharge. Because of the persistent pain the patient was examined in the clinic for neurologic diseases, where it was noted that the right pupil was smaller than the left and that it did not react as well to light or in accommodation. The palpebral fissure was narrower on the right side, and there was partial ptosis, although the eyelid could be moved voluntarily. There was no enophthalmos, and there were no vascular changes on the face. It was assumed that the pain and the Horner syndrome were due to injury to the right sympathetic trunk at the time of the operation.

Case 9.—V. G., a girl aged 19, was first admitted to the University Hospital in August 1932 because of hemoptysis. A diagnosis of moderately advanced tuberculosis of the upper field of the left lung was made, and the patient was treated with artificial pneumothorax: a temporary interruption of the left phrenic nerve was made in December 1932 and an attempt at permanent phrenicectomy in August 1933. Apparently a minor accessory branch of the phrenic nerve was not sectioned, and motion returned in the diaphragm. On readmission to the hospital in July 1934 it was deemed advisable again to attempt permanent exeresis, and the operation was performed by Dr. John Alexander. He found two small accessory nerves, which he resected, and then, on searching further, found posterior to the internal jugular vein a nerve of moderate size which might have been a far mesial phrenic nerve trunk. However, as there were several small branches passing both mesially and laterally from the nerve, he believed it to be the sympathetic trunk. In order to make the differentiation he pressed it lightly before anesthetizing it, and this did not cause hiccup. He then injected a small amount of solution of procaine hydrochloride, which caused contraction of the pupil on the same side. Postoperatively it was noted that the patient had miosis and partial ptosis on the left side, and the conjunctival vessels on this side were dilated and engorged. When the patient was last seen seven weeks after the operation these signs had almost completely disappeared, and the difference in the size of the pupils was barely discernible.

Case 10.—F. R., a woman aged 37, was admitted to the hospital with a diagnosis of advanced pulmonary tuberculosis. Roentgen examination showed bilateral apical pulmonary tuberculosis with gross cavitation and infiltration of the left lung. Following a third stage thoracoplasty by Dr. John Alexander there was such paradoxical movement of the anterior lower thoracic wall that temporary paralysis of

the phrenic nerve was performed at once. The main stem of the nerve was crushed, and in the search for another root a nerve lying on the mesial edge of the scalenus anticus muscle was lightly crushed. Following the operation miosis and partial ptosis were noted on the left side. When the patient was last seen, three weeks after the operation, there was some improvement in the condition.

CONCLUSION

Enumeration of the cases of Horner's syndrome that have been observed during the past year would lead one to agree with the observers who state that paralysis of the cervical portion of the sympathetic nervous system, in full or in part, is more frequent than the literature indicates.[20] Cases of incomplete paralysis and those of minor involvement may easily be overlooked. In cases reported here the etiologic factors underlying the syndrome could be determined definitely. This is in disagreement with the statements in the literature to the effect that the causative factors usually are obscure or cannot be found.[21]

SUMMARY

Ten cases of Horner's syndrome observed during the past year are reported.

Horner's syndrome follows either a disease process or trauma, accidental or surgical, which involves some portion of the cervical part of the sympathetic nervous system.

The cases herein reported illustrate Horner's syndrome occurring in cases of tumor of the spinal cord, syringomyelia, cervical pachymeningitis, aortic aneurysm, tumor of the upper part of the pulmonary sulcus, dislocation of the cervical vertebrae, metastatic mammary carcinoma and complicating thyroidectomy and phrenicectomy.

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20. Scarlett, H. W.: Frequency of the Claude Bernard-Horner Syndrome, Am. J. Ophth. **11**:961 (Dec.) 1928.

21. Fuchs, H. E.: Textbook of Ophthalmology, translated by Alexander Duane, Philadelphia, J. B. Lippincott Company, 1917, p. 452. Scarlett,[20]

ACOUSTIC IMAGINATION AND ACOUSTIC HALLUCINATION

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Acoustic imagination has always attracted the attention of psychologists. Charcot distinguished three types of imagination in human beings: the optic, the auditory and the motor. It is generally supposed that the acoustic and the motor types are closely related to each other. Baerwald,[1] in a study of image types, mentioned acoustic imagination. Almost every textbook of psychology refers to the subject. No special attention has, however, been given to the topic of voluntarily produced auditory images and their characteristics. The studies of Jaensch and his school on eidetic images have revived interest in the world of imagination. As is well known, eidetic images possess many of the qualities of perception and take a position between representation and perception. Henning[2] found that there are fixed and mobile eidetic pictures in the auditory as well as the optic sphere. He stated that "at times the acoustic image remains stable and unchanged for several seconds or even minutes at a time." One of his subjects said: "The word is enormously stretched, as it were. It is continuously expressed without, somehow, actually being repeated." To six of thirty academic subjects in Henning's experiments the imagined word seemed to be within the auditory meatus instead of in outer space and remained fixed there for some time. Henning spoke only of eidetic images, but the borderline between eidetic images and representation is, as one of us (P. S.) has repeatedly pointed out, not sharp.

We began our studies on acoustic imagination not so much in order to fill a gap in the literature, but in the course of a systematic investigation of the qualities of imagination in the different senses. Kanner and one of us (P. S.)[3] studied optic imaginations, with special refer-

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1. Baerwald, R.: Zur Psychologie der Vorstellungstypen, Leipzig, Johann Ambrosius Barth, 1916, p. 444.

2. Henning, H.: Starre eidetische Klang- und Schmerzbilder, Ztschr. f. Psychol. **92**:137, 1923.

3. Kanner, L., and Schilder, P.: Movements in Optic Images, J. Nerv. & Ment. Dis. **72**:89 (Nov.) 1930.

ence to their relation to movements. Bromberg and one of us (P. S.) [4] studied the images in the fields of touch, smell and taste. In the tactile and optic spheres voluntarily produced images exhibit properties which correspond closely with primitive perceptions and with perceptions which occur after lesions of the central nervous system. An intimate relation has also been found, especially in the tactile sphere, between the qualities of after-effect and imagination. There is further, an interrelationship of perception of short duration, after-effect and imagination. Olfactory and gustatory images are closely interwoven with vegetative phenomena. In the senses thus far examined it has been found that the image more easily leads back to the primitive foundation of experience, thus revealing the basis on which perception has been built. These studies have therefore offered the possibility of increasing insight into the phenomena of perceptions and, especially, of hallucinations. They point, furthermore, to the common background of imagination, hallucination and perception.

Experiments on the influence of vestibular irritation on optic and tactile imagination and after-effects (giving almost identical results in the perceptual and image fields) added further proof of the inherent unity of perception, after-effect, imagination and hallucination. Imagination, perception and hallucination follow the same laws. All of them can be influenced through the somatic agency of vestibular irritation. The hallucination brings those parts of perception and imagination into the foreground which in the normal person have remained in the psychic background. Organic change in the central nervous system has the same effect. Shortening the duration of sensual perception in normal persons also provokes phenomena which are similar to the background experiences of normal persons, to hallucinations and to the altered perceptions of those suffering from organic lesions of the brain.[5] On the other hand, previous studies had shown that it was not possible to transfer conclusions from studies of one sensory field to another field of sensory experience. The results obtained on smell and taste revealed a different picture from those obtained in the visual and tactile spheres. We had, therefore, good reason to pay closer attention to the findings in the auditory field.

METHOD

We examined eight subjects between the ages of 25 and 40. One was not a physician. They were first requested to produce voluntary auditory imaginations.

4. Bromberg, W., and Schilder, P.: (*a*) On Tactile Imagination and Tactile After-Effects, J. Nerv. & Ment. Dis. **76**:1 (July); 133 (Aug.) 1932; (*b*) Olfactory Imagination and Olfactory Hallucinations, Arch. Neurol. & Psychiat. **32**:467 (Sept.) 1934.

5. Schilder, P.: Experiments on Imagination, After-Images and Hallucinations, Am. J. Psychiat. **13**:597 (Nov.) 1933.

In a second series of tests with the same subjects the after-effects of sound were studied. In a third series imagery was studied after acoustic stimuli were offered. In a fourth series we examined the influence of rotatory vestibular effects on perceptions, after-effects and imaginations in the acoustic sphere. In conjunction with the experimental data we investigated suitable auditory hallucinations, comparing particularly the hallucinations of patients with alcoholism with those of patients with schizophrenia.

The instructions for the tests of voluntary imagination were to imagine: (1) somebody talking, (2) a loud cry, (3) the hum of a crowd of people, (4) the crack of a whip and (5) the noise of a siren.

The after-effects studied were: (1) the human voice (counting), (2) tuning fork C-512, (3) the noise apparatus.

We used the Bárány turning chair to produce vestibular stimulation. The same list of perceptions, after-effects and images already given were then studied under this influence (that is, after the turning ceased). Our subjects used the term memory image when the sensual qualities were pale; when these were better defined they spoke of representation and image. We have not used the term "eidetic image," but have made note of outstanding sensual qualities in the protocols.

OBSERVATIONS

All our subjects were able voluntarily to produce auditory images. The acoustic image was, however, usually linked to an optic one.

Protocol A.—Subject P., when imagining some one talking to him, said: "It is difficult to get the actual acoustic image; it is rather an auditory memory. The image has the characteristics of the particular person's voice, however. The whole is much less acute and clear than reality or perception. The visual image is more powerful and always accompanies the auditory one. The voice appears always to remain at the same distance from me, but this seems to be governed by the distance of the visual image. I do not get the voice image without the visual image."

Protocol B.—Subject Str., when imagining the crack of a whip, said: "There is a gradually increasing sound and optic image. I imagine it to be right ahead. There is a noise in the ears and it is felt there, but only at the time a noise is being made. I actually see the whipping in a setting of its own, e. g., a lion-tamer in a lion's den."

Protocol C.—Subject S., when imagining a loud cry, said: "I feel it in the ear: a dramatic cry of a woman which I imagine visually. It disappears and has to be renewed. It comes to the ear as a radiation, coming to a point. The optic image remains more steady than the sound. I have to renew the optic image if I want to keep the sound." When the same subject tried to imagine the voice without a visual image, he said: "Some sound floats around in space and the feeling of talking in one's own throat is increased."

Protocol D.—Subject M., when imagining a noise without an optic image, said: "I hear a momentary blast, like a deafening and intense crack of something—like an enormous firecracker right near my ear. I also hear a muffled sensation, like dynamite blasting in the earth. I feel it also directly in my ear."

Although optic imagination generally leads to the acoustic image, independent auditory imagination is possible, though more difficult.

Protocol E.—Subject C. first imagined the sound of a C-512 tuning fork with an optic image and then received the order to imagine the same tone without the

visual image. He said: "It is very different from the foregoing image with the sensation as of cotton in the ears. Only for a moment is there a sharp sensation of sound."

As protocol A shows, the acoustic image is localized at the distance of the visual image. The following protocols show the path the sound takes on the way to the ear.

PROTOCOL F.—Subject H., when imagining a crowd talking, said: "A mob is shouting at the inauguration of a president or at a guillotining or at a political meeting. There are shifting, unclear optic images. I see the motions of groups, as if fighting is going on, and hear primitive noises and shouts, such as 'Hurray.' The sound is associated with the visual images, but neither is heard in the ears, nor do the sounds seem to come toward the ears. There is no sensation of space being filled. I see small units of people. Vague murmuring is a background for occasional shouts."

PROTOCOL G.—Subject H., when imagining a siren sounding, said: "I visualize an old-style fire engine; also, a motor boat. I hear the noise of the exhaust. I visualize a factory whistle and the escaping steam, and the sound varies according to the optic image. The auditory images recur three or four times with the visual image. The acoustic images are directly before me. They come directly to my ears from the object, like a beam, without spreading. Space does not seem to be filled."

PROTOCOL H.—Subject S., when imagining the crack of a whip, said: "I see the whip at my side. I hear the sound there and it passes into my ear. It has to be brought back to the whip. There is a dissociation between the optic image and the sound. The sound seems to wander, has an unclear, irregular outline and has to be renewed. There is a tendency to produce a special setting for the sound: horses, grass, boys. There is a short sound as of the cracking of the whip; but it can't be retained; it has to be repeated. It is like machine-gun fire when I make an effort to retain it."

PROTOCOL I.—Subject S., when imagining the sound of a tuning fork, said: "The sound seems like a jagged area in space, diffuse and shredded."

PROTOCOL J.—Subject E., when imagining the cracking of a whip, said: "This image gives more of the feeling of pure sound, but it seems to be filling space all around, or to be multiplied in space. The auditory image is clearer than in the other types."

PROTOCOL K.—Subject E., when imagining the blowing of a siren, said: "I have more the feeling that the air is filled with sound. I can't keep the sound continuous; the revival of the auditory image takes place only with great effort."

PROTOCOL L.—Subject B., when imagining a crowd, said: "I make the noise 'whoopee.' I feel it in my lips. I see an ocean of heads. They form a background for me making the noise. I feel a tension in my own throat and lips, but of the crowd I can only feel their restlessness. There is only a very faint auditory image which soon returns. If I pick out one of the crowd to holler, it soon becomes my voice."

PROTOCOL M.—Subject Str., when imagining the sound of a siren, said: "The screeching gets into my ears. I can retain the intensity if I don't breathe. It comes to me in rhythmic thrusts."

PROTOCOL N.—Subject Str., when imagining the sound of a tuning fork, said: "It remains regular in sound. I hear it at the tip of my nose. It is rhythmic."

PROTOCOL O.—Subject M., when imagining some one talking, said: "I imagine a girl-friend talking to me over the 'phone. I feel something like a voice in my ear. I have no other sensation. I feel as if I were saying single words in answer."

PROTOCOL P.—Subject S., when imagining some one talking, said: "I feel the voice at my side. It is easier to imagine it in relation to some particular person. It seems to repeat itself. The sound travels about in the form of a circle."

PROTOCOL Q.—Subject S., in a repetition of the preceding test, said: "G. is sitting in a distant office. I have an auditory image of his voice saying 'R. will be elected.' I have a tendency to repeat it in my own throat. The sound rushes away from him and seems to come nearer to my own throat. But I imagine the distant office right where I am standing."

PROTOCOL R.—Subject C., when imagining a voice, said: "X's voice is shouting. We are somewhere else. The voice is far away. It changes to the voice of others which are also far away. I am at all the other places."

The imagined sound seems to remain in its place or to travel through space, either in the form of a beam or a circle on the one hand, or like a jagged, irregular area on the other. It may go into the ear. Besides the sensation of sound it may also provoke there a tactile feeling. That depends to some extent on the type of sound which has been imagined. When voices are imagined the sound seems to wander to the throat of the subject, and finally definite words are formed and the acoustic imagination is connected with the motor activity. In the different protocols the various stations along this road are emphasized, partly depending on the attitude of the subject and partly in accordance with the character of the imagined sound. Almost invariably the imagination of voices is connected with movements in the subject's own throat for the formulation of words. The sound is usually imagined at the distance at which sounds of this type are generally heard. Protocols Q and R may be considered remarkable in this respect because the sound (speaking) is imagined at a great distance, beyond the range of the ordinary speaking voice. But in both cases the subject imagined himself at speaking distance from the imagined voice, in the one case as having been transported to the imagined place and in the other, as having the imagined setting brought to the room in which the experiments are being conducted.

PROTOCOL S.—Subject P., when imagining a voice, said: "A train-caller announces departures. I have a visual image of the Grand Central Station with an auditory image of a monotonous, radio-toned voice filling the air. The words are a jumble except when there is some sensation of speech in my own larynx. There is no clarity of hearing. The acoustic image fades and returns. The visual image sticks better. The auditory image is before me."

One finds the definite rule that when actual words are imagined the words are formed in one's own mouth. This occurred with all our subjects.

The protocols show clearly that the auditory image does not change its quality or pitch. It also fades away gradually or disappears suddenly.

PROTOCOL T.—Subject C., when imagining a tuning fork, said: "I have a visual image of myself striking the tuning fork. At first there is a loud, high-pitched tone which fades; I have no feeling in the ear. The ear does not feel full, and the image is less distinct than the after-image. I have to repeat the visual image to keep the auditory image." (Compare this with protocol B.)

The acoustic image has to be revived (protocols K and C). But there is a spontaneous tendency to repetition and multiplication (protocols J and P). These repetitions and multiplications often have a rhythmic character (protocols already cited and the ones that follow).

PROTOCOL U.—Subject S., in describing the after-effect of a C-512 tuning fork, said: "There were about four rhythmic repetitions. With each repetition, the sound seems to come closer to the ear. A feeling of fulness is present in the ear. It revives and fades, depending on the concentration one gives to it. It is very simple to imagine the same thing after the after-effect has faded." (At another time the same subject heard the after-effect seven or eight times.)

PROTOCOL V.—Subject C., in a similar experiment, said: "There is a sharp and filling sensation in the ear which becomes less and less distinct. The after-effect is a distant, low hum which is less distinct than the actual sensation of lower pitch."

All the subjects could revive the acoustic image easily after the after-effect had worn off. The results of our experiments on after-effects with the noise apparatus were practically identical with those just described. The after-effect was more like rhythmic waves of short amplitude, more diffuse in space than the perception itself (protocol W).

PROTOCOL X.—Subject Str., in the test with the noise apparatus, said: "The impression of grinding wheels gave it a rhythm it didn't have. It lasted no more than fifteen seconds."

Subject C. linked the rhythm of the after-effect with his breathing. The following protocols on the after-effects of the human voice deserve special mention, however.

PROTOCOL Y.—Subject P., with the test of the experimenter counting to 5, said: "The immediate after-effect is a sort of reverberation closely associated with the ears and having the characteristics of the examiner's voice. This diminishes in intensity, becomes difficult to retain steadily and finally merges with the qualities of an image of the examiner's voice which has less clarity than the immediate after-effect." (The results were practically the same when the examiner emitted a continuous sound instead of counting.)

PROTOCOL Z.—Subject S., with the same test as in protocol Y, said: "The sound of 5 persists for a while, then fades into a hissing and then to nothing. Reviving the image produces the feeling of counting oneself, but with the quality

of the examiner's voice. Every effort to get the auditory image back again is connected with a feeling of counting in my own throat. At the same time, the sound comes nearer."

When, instead of counting, a continuous sound was emitted by the examiner, there is less of a tendency to utter the sound oneself. There is no immediate after-effect, but one can recall it as a quite vivid after-image. Then it fades out and is distributed widely in space. Every new repetition is paler and more diffuse. The final distribution in air seems irregular and shredded.

ROTATORY EXPERIMENTS

The Effects of Vestibular Irritation.—The vestibular stimulus we used in the course of these experiments was the after-effect of rotation in the Bárány turning chair. It proved too difficult to make observations during the turning procedure itself, which consisted of from three to ten turns from left to right. We found it advisable not to turn the subjects too many times, since too great dizziness makes imagination much more difficult and obscure. The source of sound was always at a distance of about 6 feet (182 cm.) to the right of the subject, and the sounds used were the tuning fork, the noise apparatus and the human voice. In the first series of observations the subject was sometimes exposed during the turning, but the period of examination of the effect on auditory perception began after the chair had been stopped at the starting position. In a second series of tests the influence of this vestibular irritation (the after-effect of turning) on acoustic after-effects was studied. In a third series the subjects were requested to imagine auditory phenomena immediately after the chair had stopped turning.

When the chair is stopped, an apparent movement in the subject's body sets in. The subject feels as if he is turning in a direction opposite to the actual turning, i. e., from right to left. But it would be erroneous to think that the subject feels the whole body turning. Those parts of the body which are in actual contact with the chair and also a part of the heavy mass of the body are felt in their original position. What appears to be turning in the counterdirection is an indistinct, heavy mass, the borderlines of which are shadowy but seem to follow the outlines of the body. On another occasion we have spoken of the phantom of the body. Since this phantom turns to the left (when the turning of the chair stops), it leaves the sound at the right in its previous absolute position which does not change. The phantom of the body changes its position with relation to the sound, so that the source of the sound seems farther back with respect to it. When the after-effect of turning to the left fades the phantom returns to the body which has remained in its original position, and the stimulus now seems to be closer again with respect to the phantom in which one localizes oneself. It is this phantom, therefore, which determines the localization of the sound. The same principle holds true for acoustic imagination. The auditory image localized to the right recedes relatively at first (after the left-right turning is stopped) and then still farther to the right (as the phantom moves to the left) and later again appears at its original distance from the imagined source of sound (as the phantom returns to the right). Subject C. occasionally localized the auditory image in relation to his own body instead of with respect to the surroundings. As a result, his acoustic image turned with the phantom to the left in the first after-effect. This subject experienced changes in the intensity of the imagined sound whenever an apparent movement of the body took place.

COMMENT

It is well known that there is such a thing as an optic horizon at which the world seems to end, but not much attention has been given to the fact that there is also an acoustic horizon. One is surrounded by an indistinct sphere of noises. Approximately, the acoustic horizon is about as far distant from the subject as the human voice carries. This acoustic boundary is always the background from which the individual auditory experiences differentiate themselves. The sound may come from any point between the subject and this acoustic horizon. Imagination is closely bound to this structure of the acoustic world, and the auditory space of imagination also has an acoustic limit. In some of our protocols (Q and R), however, the sound is imagined as coming from a great distance, beyond the range of the ordinary speaking voice. In both of these cases, nevertheless, the subject imagined himself at speaking distance from the imagined voice. In one case the subject was transported to the imagined place and in the other the imagined setting was brought into the experimenting room.

Although initially the acoustic world of imagination is closely linked with the optic, it soon achieves a separate existence. The auditory type of imagination is generally less stable than the optic type. It is particularly difficult to retain acoustic images for any great length of time (protocol C). If one wants to keep the sound intact one has to renew the optic image. But besides this more or less voluntary effort which leads to the multiplication of sound there is also a spontaneous multiplication of sound in space (protocol M), and these multiplications often have a rhythmic character. Henning [2] observed persistent acoustic images, but according to our protocols this is certainly the exception. We secured persistent auditory imagination only when a continuously changing acoustic object, such as a crowd of people, was imagined; but there was also a continuous change in the acoustic images. Not only does auditory imagination dissociate itself in some instances from the optic image after a time, but it is possible for some subjects to achieve acoustic imagination directly and without the aid of the visual image. The acoustic image does not show any change as long as it persists. It disappears suddenly or in a gradual fade-out. The localization of the sounds depends on the localization of the optic images. When the latter lose their importance or are not present, every-day experience determines the localization of the sound. This is then usually imagined at a distance at which sounds of this type are generally heard. This imagined sound seems either to remain in its original place or travels through space. In the latter case its form may be that of a beam or a circle or like a jagged, irregular mass. It may also enter the ear. There, it may provoke something like a tactile sensation besides the sensation of sound. That depends greatly on the type of sound which has been imagined. When voices are imagined

the sound seems to reach the throat, and then definite words are formed in the throat of the subject, thus terminating the acoustic imagination in a motor activity. The protocols emphasize the different stations of the sound as it traverses this road. The controlling factors are the attitude of the subject and the character of the imagined sound. Imagined voices are almost invariably connected with movements in the subject's own throat, formulating words. When, for example, the sound of a tuning fork or the crack of a whip is imagined, some subjects also imagine that they themselves are producing the sound. They imagine themselves either striking the tuning fork or wielding the whip.

When one compares these findings with imagination in the optic sphere one discerns considerable difference. Optic imagination has a greater tendency to change its quality. It does not wander toward the subject. The motion remains within the picture. There is no motion toward the subject. The same is true of tactile imagery and of taste. In gustatory images the object of taste is relatively stable, and the taste itself is a stable quality within the subject. As in the case of sounds, however, smells approach the subject from without, and there is a movement of both sounds and smells toward the subject. Every sensory field and every sensory imagination has its specific motion. In the imaginations this movement comes to the fore with great clarity. In the optic and tactile spheres the activity remains largely within the picture. In the gustatory field the motion consists in chewing and there are especially strong salivatory, secretory and other vegetative effects. Smelling is intimately connected with the inspiration of air. In the auditory sphere the tendency to produce the sound oneself is predominant. Vestibular irritation is connected with motion inside and outside the body and with a multiplicity of motor-tonic phenomena. Thus, every sensory field has its specific motility which is not less manifest in the imaginations than in the perceptions. One can even state that these motor factors in the sensory field achieve a particularly pregnant expression in imagination (Kanner and Schilder,[3] Bromberg and Schilder,[4] Schilder [5]). Baerwald [1] specially emphasized the motor type in imagination, but the experiments we have described show that there is a motor element in every field of imagination, and it is thus questionable whether any sharp division into arbitrary types is possible. In the spirit of G. E. Mueller, we are of the opinion that the images used depend largely on the situation and not altogether on the individual subject. But Baerwald was correct in saying that the imagination of the human voice is almost invariably linked with tendencies to form words oneself. Watson [6] stated: "What the psychologists have

6. Watson, J. B.: Behaviorism, New York, W. W. Norton & Company, Inc., 1930, p. 240.

hitherto called thought is, in short, nothing but talking to ourselves." Our experiments, obtained by the introspective method and demonstrating the universal importance of motion and motor factors in images, offer some justification for this statement.

We have spoken of acoustic imaginations, but we have repeatedly stressed in the protocols that the auditory imagery occurred in a specific setting which not only was acoustic but included also imaginations from other senses. The world of imagination and the world of reality are never merely acoustic or purely optic, gustatory, olfactory or tactile. They comprise all the senses at once. Bromberg and one of us (Schilder) [4] have shown that the after-affects of actual touches are, in many respects, identical with tactile imagination. The school of Jaensch has repeatedly pointed to the intimate connections between after-effects and eidetic images. In the after-effects of sounds one finds rhythmic repetitions. With each of these repetitions the sound seems to come closer to the ear. The rhythmic character of the after-effect and the imagination demonstrates an inner relationship between the two. This relationship becomes particularly evident when one considers the fact that immediately after the fading of after-effects imagination is especially easy. This corresponds with results obtained in all other sensory fields (Bromberg and Schilder [4b] on smell). Foerster and Loewi [7] showed that sensation could be suggested in anesthetic areas resulting from organic lesions of the central nervous system in which some latent, subliminal perception was retained, but not in those areas in which perception was completely absent.

Acoustic perception, after-effects and imaginations are often coupled with local tactile sensations in the ears. As already stated, an isolated auditory world does not exist. As in the case of imaginations, auditory after-effects are connected with motor impulses.

The interrelation between the different senses becomes more clear when one exposes the subject to vestibular irritation in the course of acoustic after-effects and imaginations. The sound is then localized according to the apparent movement of the body. It retains its absolute position in space but stands in a different relation to the body because the body of the subject (or at least a part of it) is experienced in the apparent movement. This simple formulation is accurate also for perceptions during such vestibular irritations, as Allers and Benesi [8] and we ourselves have found. It should be substituted for the complicated theories which Reinhold and Alt [9] developed on this subject.

7. Foerster, O., and Loewi, M.: Ueber die Beziehungen von Vorstellung und Wahrnehmung, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:658, 1932.

8. Allers, R., and Benesi, L.: Zur Frage nach der Wahrnehmung der Schallrichtung, Ztschr. f. d. ges. Neurol. u. Psychiat. **76**:18, 1922.

9. Reinhold, J., and Alt, L.: Die Bogengänge als anatomische Grundlage, Jahrb. f. Psychiat. u. Neurol. **34**:322, 1913.

These authors expressed the opinion that the direction of sound is perceived by the semicircular canals. But our results are more compatible with the general principles stated by Leux,[10] who showed that the median localization of sound depends on righting reflexes.

Auditory Hallucinations in Twenty Persons with Alcoholic Hallucinations

	Number of Voices			Rhythm		Music		Noises		Distance		
Case	One	Several	Many	Rhythmic	Non-rhythmic	Musical	Non-musical	Types	Multiple	Ear	Near	Distant
1	..	..	+	+	..	+	..	Kicking, booming	..	..	+	..
2	..	+	..	+	..	..	+	Ticking, radio	..	..	+	..
3	..	+	..	+	..	+	+	Clicking	..	..	+	Underneath
4	..	+	+	Repeated at times	+	..	+	..	..	+	+	..
5	..	+	..	Repeated	+	..	+	..	..	..	+	2 feet; 100 yards
6	+	..	..	..	+	..	+	Whisper, radio wave	..	..	+	Behind
7	..	..	+	Repeated	..	..	+	..	..	+	+	Above
8	..	+	..	Repeated	..	+	+	Buzzing	Loud and low	+	8 feet	Many blocks
9	..	+	..	Repeated	..	..	+	..	..	..	+	..
10	..	+	..	..	..	+	..	Barking, voices	..	..	+	..
11	..	+	..	Repeated	..	..	+	..	..	..	+	..
12	..	..	Millions of voices	Repeated	..	+	+	..	In streets		+	..
13	..	+	50	Repeated	..	..	+	Bells	..	..	+	..
14	..	+	..	..	+	..	+	Shots	..	..	+	..
15	..	+	..	Repeated	..	..	+	..	..	..	+	..
16	..	+(4)	..	..	+	..	+	Like slurred speech over radio	Outside	..	+	..
17	+	..	..	Repeated	..	..	+	..	..	+	..	..
18	..	+	..	..	+	+	+	Singing telewaves	..	+	+	..
19	..	2	..	Repeated thoughts	..	..	+	..	..	+	+	..
20	..	+	..	..	+	..	+	Breaking bottles, whistles, whispers, crashes	Baby crying	..	..	Far away

AUDITORY HALLUCINATIONS

It is the general intention in this series of investigations on imaginations and after-effects to show that the pathologic phenomena occurring after lesions of the central nervous system as well as hallucinations reveal the same fundamental structure as rapid (tachistoscopic) per-

10. Leux, Irmgard: Stellung und Vorstellung des eigenen Körpers, J. f. Psychol. u. Neurol. **44**:644, 1932.

ceptions, fading perceptions (after-images) and imaginations. Eidetic images in the optic sphere show fundamental analogies with hallucinations occurring in intoxications with mescaline, hashish, cocaine and alcohol. They also show analogies with phenomena observed in agnosias. Bromberg [11] in a study on tactile hallucinations found that they are based on exaggerated after-effects, whereas the sensory element was less in evidence in the tactile hallucinations of schizophrenic subjects. The tactile after-effects were almost identical with the phenomena observed after lesions of the central nervous system. According to Bromberg and one of us (P. S.) [4b] hallucinations of smell show the same basic structure as olfactory imaginations. This is also true of olfactory hallucinations which occur in lesions of the central nervous system. We were, therefore, interested in studying hallucinations of hearing in the light of the results obtained in these experiments. Accordingly, we examined a large number of persons with alcoholic hallucinosis as well as a number of schizophrenic patients with auditory hallucinations. We have tabulated the observations on twenty of the cases of alcoholic hallucinosis. The table shows clearly that the tendency to rhythm and repetition was present in the majority. It was absent in only five. As Koehler [12] pointed out, the acoustic world is chiefly nonmusical. In line with this, only five of our patients with hallucinosis heard tones, but, with the exception of one, even these patients had hallucinations of nonmusical sounds and noises. When voices were heard they were generally not isolated voices but a multiplicity of them (except in two cases). There was usually also an irregular, continuous auditory background. The noises heard belong to the group of every-day sounds of the acoustic background. In six of the cases hallucinations were localized in the ear. In the majority, however, the voices were near-by, and in only a few were they localized at a distance approximating the auditory horizon.

One easily discerns here the close correspondence between acoustic imagination and after-effect on the one hand and the hallucinations of alcoholic intoxication on the other. There is one fundamental difference, however, in that the patients were not aware of any active tendency to reproduce the sounds heard in the hallucinations themselves or to articulate the words. In this respect the auditory hallucinations more nearly approach acoustic perception of every-day life. We venture the hypothesis that the energy of the motor impulses goes to increase the intensity of the sensory phenomena. On the other hand,

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11. Bromberg, W.: Tactual Perception in Alcoholism, Arch. Neurol. & Psychiat. **28**:37 (July) 1932.

12. Koehler, W.: Tonpsychologie, in Alexander, G., and Marburg, O.: Handbuch der Neurologie, Berlin, Urban & Schwarzenberg, 1923, vol. 1, p. 419.

there has been a strong motor reaction to the hallucinations in practically all the cases we have seen.

The schizophrenic hallucination as a type is quite different, however. One of our patients said, for example: "I heard my own voice far away. I seemed to be talking in a dream." Another schizophrenic patient heard a regular conversation in the air in Brooklyn and Harlem, but added: "They say it with their minds. Your thoughts speak the thoughts of other people. They just say things to themselves." Another patient heard God from far away (up in the sky) and also in her ears. We reproduce here this classic production of a schizophrenic woman of about 30 years. She said:

> I have had dreams since I was young. Sometimes I hear sounds. I don't know whose voice it is. It has directed me in certain things. The angel of the apocalypse is one I recognized. It was directed to me to write certain words. They gave me prophecies. I heard a voice that I thought was the angel of the apocalypse when I went to Grasslands. Sometimes I can hear what a person says in the different parts of the world. You can hear it through the soul. The soul is sufficiently active. What is the difference between a corpse and a live person? You know this voice. It speaks the thing you speak—you comprehend. If I hear President Roosevelt—Herbert Hoover—Hitler—Mussolini—Litvinoff—it comes to me in my own language and I know what it is about. The angel was not visible at the time I heard this voice. I saw two tapers and part of a person. I was very sick and receiving Holy Communion, and the priest did not have the sense to give it to me. Our Lord came around in the size and form of a pelican and I opened my mouth and I presume I received the Host. If I heard Roosevelt and Hoover, they are not familiar. The voice is an awfully loud thought. I don't hear with my ears. I get the knowledge of it through the soul and it is reflected to the ear. Your senses get outside stimuli. Sometimes you get knowledge through the senses and your senses impress the soul. I get my knowledge through my soul and the soul, reflects on the senses. I went through certain performances when I opened the window and shouted. I could not make out whether or not it was a female or male voice. I felt this awful urge to do. The voice is deep and soft. At Grasslands I looked out the window and saw a cloud with God the Father, a dove and a pelican. He said: "Don't forget you have a covenant with me." God the Father was talking. In fact, I could see his lips moving. He was talking to me. That was fifteen years ago.

It is a characteristic in all such instances as the one just quoted that the voices affect the soul. Also, they do not come from the real space about one, but from symbolic space. The feeling is predominant that one's own words are being spoken. The schizophrenic hallucination has accordingly less sensory elements, on the whole, than the alcoholic hallucination, an observation which corresponds closely with Bromberg's results in the studies on tactile hallucinations. Here, too, one sees that the study of imagination and after-effects of sensations is the basis of understanding of pathologic phenomena. We do not state, of course, that hallucinations of the alcoholic type cannot occur in persons with schizophrenia or vice versa. We wish only to point out

that we were dealing here with two quite distinct types, differentiated by well characterized psychologic structures. We also do not believe that such formal investigations as these offer conclusive insight into imaginations and hallucinations. Every psychic phenomenon arises from a total personality which possesses aims and goals. A broader understanding of these factors requires a much deeper analysis of the total personality. Our investigations indicate, however, through which channels this total personality expresses itself.

SUMMARY

Voluntarily produced auditory images and their changes were studied in normal subjects and compared with after-effects. The influence of vestibular irritation on such images and after-effects was also studied.

The acoustic image is usually linked to an optic image, but auditory imagination is independently possible, though more difficult. Even when linked to an optic image the auditory one eventually separates.

The sounds are localized at the distance of the visual image, or with some exceptions, at the distance at which such sounds are generally heard. They have a tendency to travel in space and also to reach the ear.

Imagination of voices almost invariably leads to motor activity in the subject's own throat, formulating words.

Auditory images do not change quality or pitch. In our experiments they showed a tendency to fade gradually or to disappear suddenly.

There is a spontaneous tendency to repetition, multiplication and rhythm in the imagined sounds as well as in the after-effects.

Vestibular irritation provokes a phantom of the body which turns in a direction opposite to the actual turning of the chair. The absolute localization of the sounds, images and after-effects remains unchanged, but since this phantom of the body becomes the center for localization, the position of the sounds, images and after-effects changes with relation to this subjective phantom.

A study of hallucinations in persons with alcoholism and schizophrenia suggests that the toxic auditory hallucination has essentially the same structure as the imagination (although without the motor aspect), while the schizophrenic auditory hallucination is of a different type, with less sensory quality and more symbolic and motor elements.

There are differences between auditory and other types of imagery, particularly with respect to the motor components.

Every sensory field has its characteristic motility and motion.

LEFT-HANDEDNESS

INTERCORRELATIONS WITH ENURESIS AND OTHER RELATED FACTORS IN SO-CALLED NORMAL CHILDREN

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Does left-handedness, with the realization of one's difference, give rise to a certain sensitivity, or rather is it one of the pathophysiologic reactions (a "benevolent stigma") of a discordant personality? The many points of view on this problem vary from that of Bauer,[1] who considered left-handedness as a "degenerative stigma," to that of Quinan,[2] who regarded left-handedness and general sinistrality as usually indicative of constitutional instability. It would seem likely to us that more meaning and value could be derived from some of the concepts if attempts were made to correlate left-handedness with more specific and definite variables rather than with such general and indefinite concepts as constitutional psychopathic states, the epilepsies and feeblemindedness.

In an earlier paper[3] we reported our findings on the intercorrelations of enuresis and other factors in 475 so-called normal children at a camp. The data in the present study have to do with the same group but are concerned specifically with the intercorrelations of left-handedness with enuresis and other factors. Included under our term left-handedness are those persons who, originally left-handed, were changed to right-handedness and those who would be considered conspicuously

1. Bauer, Julius: Die konstitutionelle Disposition zu inneren Krankheiten, ed. 3, Berlin, Julius Springer, 1924.

2. Quinan, Clarence: The Principal Sinistral Types: An Experimental Study Particularly as Regards Their Relation to the So-Called Constitutional Psychopathic States, Arch. Neurol. & Psychiat. **24**:35 (July) 1930; Handedness and Eyedness of Speeders and of Reckless Drivers, ibid. **25**:829 (April) 1931; Sinistrality in Relation to High Blood Pressure and Defects of Speech, Arch. Int. Med. **27**:260 (Feb.) 1921.

3. Michaels, J. J., and Goodman S. E.: Incidence and Intercorrelations of Enuresis and Other Neuropathic Traits in So-Called Normal Children, Am. J. Orthopsychiat. **4**:79 (Jan.) 1934.

ambidextrous. In judging the dominance, the determining factors consisted of nativeness and of the hand used in writing, throwing, sewing and other manual practices. The methods and criteria for determining the other traits and factors were those previously described.[3]

The incidence of left-handedness is variously reported. Schiller [4] commented on the range of 3.8 per cent estimated by Kapustin in Russia in comparison with her own findings of 11.5 per cent in 2,520 boys and 7.9 per cent in 5,131 girls, left-handedness being considered in a broader sense. We found the incidence to be 11.11 per cent for our group of 468. (The sexual differences in general were not statistically significant.) Of all the traits studied, with the exception of the Chvostek sign, the incidence of left-handedness was less than that of any other (table 2).

Evidence that a higher percentage of left-handedness is apparent in younger children (from 2 to 6 years) than in older ones has been presented by Schaefer,[5] Neurath [6] and Bethe.[7] Most of the literature reviewed disclosed a slightly higher incidence of left-handedness among

TABLE 1.—*Distribution of Left-Handedness According to Age in Years*

Age	8	9	10	11	12	13	14	15	16	17
Girls	4	2	0	6	4	2	3	0	0	1
Boys	2	3	6	3	5	3	4	3	1	0
Total	6	5	6	9	9	5	7	3	1	1

the male sex. Table 1 shows the distribution according to age of the 52 left-handed children in our group. The mean age did not differ appreciably from the mean age of the entire group.

In our previous paper concerning the occurrence of enuresis in relation to other neuropathic traits [3] it was shown that five neuropathic traits—enuresis, nail-biting, thumb-sucking, temper tantrums and speech impediments—tended to occur more often in combination than in isolation and that enuresis might be regarded as a possible common indicator of this type of symptom complex. It was also noted that enuresis was found to be associated with maladjustments of both "lower" and "upper"

4. Schiller, Maria: Probleme um die Linkshändigkeit mit Untersuchungen an Stuttgarter Schulkindern, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:496, 1932.

5. Schaefer, M.: Die Linkshändern in den Berliner Gemeindeschulen, Berl. klin. Wchnschr. **48**:295 (Feb. 13) 1911.

6. Neurath, Rudolf: Ueber Linkshändigkeit im Kindesalter, Wien. klin. Wchnschr. **35**:895 (Nov. 16) 1922.

7. Bethe, Albrecht: Zur Statistik Der Links- und Rechtshändigkeit und der Vorherrschaft einer Hemisphaere, Deutsche med. Wchnschr. **51**:681 (April 24) 1925; A Survey of Left-Handed Students, Berlin letter, J. A. M. A. **102**:308 (Jan. 27) 1934.

levels of the personality and that seemingly it is a reflection (individuation) of an ill-balanced personality (faulty integration of the components of the different levels). Therefore, one may assume enuresis to be a specific variable of the personality with important clinical significance.

The percentage of left-handedness in relation to the presence or absence of enuresis and other traits and factors is given in table 2. This table shows the various traits and the percentage of their general incidence. Columns 3 and 4 show, in percentage, the presence and absence of these traits, respectively, in relation to left-handedness. Column 5 shows the difference in these percentages with the standard deviation. Column 6 shows the difference of the presence and absence of these traits in percentage in relation to enuresis.

TABLE 2.—*Percentage of Left-Handedness in Relation to the Presence or Absence of Enuresis and Other Traits and Factors*

Trait	General Incidence	Present	Absent	Difference in Relation to Left-handedness	Difference in Relation to Enuresis
Left-handedness	11.1	....	....	.....	−11 ± 5.7
Enuresis	24.7	6.5	12.7	−6.2 ± 2.9	.....
Thumb-sucking	25.5	12.5	10.9	+1.6 ± 3.5	+12 ± 5.2
Nail-biting	51.3	11.0	10.7	+0.3 ± 2.9	+12 ± 4.0
Speech impediments	20.0	12.0	11.0	+1.0 ± 2.0	+17 ± 5.7
Temper tantrums	14.5	8.0	11.0	−3.0 ± 3.9	+14 ± 6.5
Sleep disturbances	19.1	9.8	11.2	−1.4 ± 3.7	+ 5 ± 5.5
Dreaming	52.0	9.4	12.5	−3.1 ± 2.9	+ 1 ± 4.1
Chvostek sign (boys)	6.9	21.4	14.6	+6.8 ±13.5	.....
Failures in school	22.4	9.7	11.5	−1.8 ± 3.3	+17 ± 5.5
Familial left-handedness	34.9	15.0	9.5	+5.5 ± 3.5	− 3.1± 4.2
Familial enuresis	23.2	6.8	12.9	−6.1 ± 3.2	+20 ± 5.5
Familial twins	16.4	12.5	10.2	+2.3 ± 4.4	− 9 ± 4.8

Our findings on enuresis do not confirm those of Stier,[8] who reported an incidence of enuresis of 17.4 per cent in left-handed, in contrast to 9.7 per cent in right-handed, soldiers. In left-handed military prisoners he found an even higher percentage of enuresis (27.5 per cent). We found the percentage of enuresis with the presence of left-handedness to be 15 per cent and with the absence of left-handedness (i. e., with right-handedness) to be 26 per cent—a difference in percentage of −11 ± 5.7. Or to state the results in another way, the difference in the presence of enuresis and its absence in relation to left-handedness was −6 ± 2.9 per cent.

Thumb-sucking, nail-biting, temper tantrums, sleep disturbances and dreaming showed no significant associations with left-handedness.

8. Stier, E.: Untersuchungen über Linkshändigkeit und die funktionellen Differenzen der Hirnhälften, Jena, Gustav Fischer, 1911.

Travis[9] in his basic textbook, reviewed numerous contributions relative to the association of left-handedness and the presence of speech impediments and concluded that in general there is a higher incidence of speech defects among the left-handed, and more particularly among those shifted from native left-handedness to acquired right-handedness. In our findings there was only a very slight difference in percentage— $+1 \pm 2.0$ (not statistically significant). This does not favor the association of left-handedness and the presence of speech impediments.

We found no appreciable association between the presence of a positive Chvostek sign and left-handedness among the boys.[10]

Wiseley,[11] in a study of 18,560 elementary school children, reported that 6 per cent of the right-handed children were repeaters, whereas 12 per cent of the left-handed ones were repeaters. Our percentage was smaller (9.7) among the left-handed children who had a record of failures in school than among those who did not fail (11.5). Computing our results in a manner similar to that of Wiseley, 22.4 per cent of the right-handed children failed, while only 19.2 per cent of the left-handed children failed (repeated).

The inheritance of left-handedness has often been postulated. The literature has been well covered by Schott.[12] In our series of 475 children there was a familial incidence of left-handedness of 34.9 per cent. When this familial incidence is compared with left-handedness in the child, a slight but not significant tendency toward association is found. This is in contrast to the definite association of enuresis in the child and in the family; the difference in percentage between the presence of familial enuresis and its absence among the enuretic children was 20 ± 5.5. In general, one might have expected a greater association of left-handedness in the family and in the child than is indicated by our findings. Whether the inclusion of the ambidextrous children played a rôle in lowering this might warrant consideration. The familial history of the left-handed children seemed to have no relationship to the presence or absence of enuresis in the child.

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9. Travis, L. E.: Speech Pathology, New York, D. Appleton and Company, 1931.

10. In view of the possible relationship of calcium deficiency to neuromuscular irritability, it may be interesting to mention here that Michaels and Searle (The Calcium of the Cerebrospinal Fluid, Blood Serum and Serum Ultrafiltrate in Relation to the Clinical Findings in Eighty Neuropsychiatric Patients, Arch. Neurol. & Psychiat. **33**:330 [Feb.] 1935) found no differences in the calcium of the blood serum and of the spinal fluid and the filtrate calcium of the blood serum in 9 left-handed and 71 right-handed neuropsychiatric patients.

11. Wiseley, W. G.: A Study of the School Progress of Left-Handed Children, Ohio Schools, April 1930, p. 144.

12. Schott, Adolf: Linkshändigkeit und Erblichkeit, Ztschr. f. d. ges. Neurol. u. Psychiat. **135**:305, 1931.

The theory of left-handedness in relation to twinning has been given weight by Newman [13] and by Wilson and Jones [14] among others. We found the familial incidence of twins in our whole group to be 16.4 per cent. No significant association was discovered between the presence of a familial history of twins and left-handedness in the children.

In view of the many claims that left-handedness is related to neuropathic and psychopathic types of personality, our findings, which point rather to a lack of association of left-handedness with those factors that might be regarded as indicative of "nervous instability," are not corroborative. Previously, we emphasized the presence of enuresis as one of the important "indicators." The contrast between the association of left-handedness and of enuresis with these factors becomes more evident and forceful when the difference of percentage in the presence and absence of traits in relation to left-handedness (table 2, column 5) is compared with the difference of percentage in the presence and absence of traits in relation to enuresis (table 2, column 6). As already noted, we found no significant constellations with left-handedness, whereas with enuresis the tendency toward positive and significant associations was striking.

Why should enuresis be more indicative of an ill-balanced personality than left-handedness? It might be suggested that enuresis seems to have its roots more in the "instinctual" sphere, left-handedness more in the "cultured" sphere, of the personality. The differences we found in the hereditary implications between enuresis and left-handedness may be regarded as not without value, particularly since the history of familial enuresis in relation to enuresis in the child was much more evident than was the history of familial left-handedness in relation to left-handedness.

CONCLUSIONS

1. A negative but insignificant statistical association was found between left-handedness and the presence of enuresis, temper tantrums, sleep disturbances, dreaming and failures in school.

2. A very slight positive but insignificant statistical association was found between left-handedness and the presence of speech impediments, thumb-sucking, nail-biting, the Chvostek sign, a familial history of left-handedness and a familial history of twins.

3. A familial history of left-handedness bears no relationship to enuresis in the child.

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13. Newman, H. H.: The Physiology of Twinning, Chicago, University of Chicago Press, 1923.

14. Wilson, P. T., and Jones, H. E.: Left-Handedness in Twins, Genetics **17**: 560 (Sept.) 1932.

4. Left-handedness in the child is not associated with familial left-handedness to the degree to which enuresis in the child is associated with familial enuresis.

5. Left-handedness does not appear to be as important clinically in its indication of an ill-balanced personality as does enuresis.

6. Before the acceptance of left-handedness as an indicator of nervous or constitutional instability, its relationship to specific factors more definitely indicating this state should be better established.

PROTEINS OF THE BLOOD SERUM IN CASES OF ESSENTIAL EPILEPSY

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In connection with a theory of the cause of epilepsy held by one of us (B. W. McK.) to be published later, it was of interest to investigate the proteins of the blood serum of patients having this disease. Intensive studies have been made of the blood in cases of epilepsy,[1] but no significant changes from the normal have been found. However, not much attention has been given to the serum proteins, in spite of their importance in influencing the water balance between the blood and the tissues and other possible functions not yet well understood. The few observations which have been made on serum proteins are not conclusive and seem to leave the field open for further work.

Meyer and Brühl,[2] Brühl [3] and Meyer [4] measured the albumin content of the serum in a group of sixteen patients, using the refractometric and Kjeldahl methods. They found that the values obtained by the former method were higher, and they concluded that the refractive property of the serum albumin in these patients was altered. It is now generally agreed that the refractometric method gives higher results. Wuth [5] determined the amount of serum albumin for forty patients by the refractometric method and found high values, averaging 8.3 per cent. The high values were attributed to an increase of blood pressure during the seizures, but daily measurements for three weeks showed little

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1. Lennox, W. G., and Cobb, S.: Epilepsy, from the Standpoint of Physiology and Treatment, Medicine **7**:105 (May) 1928.

2. Meyer, M., and Brühl, F.: Zur Pathologie des epileptischen Krampfanfalls, Ztschr. f. d. ges. Neurol. u. Psychiat. **75**:158, 1922.

3. Brühl, F.: Weitere Untersuchungen über den Serumeiweisswert beim epileptischen Krampfanfalle und seine Beziehungen zum Blutdruck, Ztschr. f. d. ges. Neurol. u. Psychiat. **83**:656, 1923.

4. Meyer, M.: Serologische Studien zur Pathologie des epileptischen Krampfanfalls, Zentralbl. f. d. ges. Neurol. u. Psychiat. **41**:726, 1925.

5. Wuth, O.: Untersuchungen über die körperlichen Störungen bei Geisteskranken, Berlin, Julius Springer, 1922.

fluctuation. Later, Wuth [6] reported an increase in the amount of albumin after seizures. Frisch and Fried,[7] using a gravimetric method, found high values for the ratio of albumin to globulin for a few patients having frequent seizures. Lennox and Cobb,[8] using the colorimetric method of Wu, found essentially normal values for a small group of patients. These reports seem to leave unsettled whether any alteration in the amount of serum proteins is shown for large groups of patients with epilepsy and whether there is any change at the time of seizure.[9] It has been the purpose of this investigation to answer these questions.

METHOD

We determined the albumin and globulin contents of the serum for a large number of patients, both those used as controls and those with epilepsy, some of the latter group being studied for several hours immediately after a seizure. The method used for the analyses was the excellent one proposed by Greenberg.[10] During the course of the study cases were separated on the basis of sex, but no significant differences were found, the average values for the albumin and globulin contents being at the most 0.05 or 0.06 per cent lower for women than for men. The specimens of blood were taken from patients at the State Hospital at Dix Hill, N. C., and were analyzed as soon as possible after being drawn; this was usually from three to ten hours.

RESULTS

The following data represent results obtained for normal patients used as controls and for patients with epilepsy, the blood from the latter subjects being taken not immediately before or after a convulsion. The time from one convulsion to the next varied from several hours to several months.

While there are slight differences in the average values, resulting in a difference of 0.15 in the ratio of albumin to globulin, for normal subjects and that for patients with epilepsy, they are obviously not

6. Wuth, O.: Bemerkungen zu der Arbeit von H. Pfeiffer, F. Standenath, und R. Weeber im Band 98 dieser Zeitschrift, Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:210, 1926.

7. Frisch, F., and Fried, E.: Zur Frage der angeblichen Alkalose bei Epilepsie, Ztschr. f. d. ges. exper. Med. **49**:462, 1926.

8. Lennox, W. G., and Cobb, S.: Epilepsy, Medicine **7**:186 (May) 1928.

9. In this connection it is interesting to note the work of R. L. Holman, E. B. Mahoney, and G. H. Whipple: (Blood Plasma Protein Regeneration Controlled by Diet: Liver and Casein as Potent Diet Factors, J. Exper. Med. **59**:251 [March] 1934.) This work, published while these studies were in progress, would seem to show that the body makes an attempt to keep the percentage of the serum proteins constant, and that before there is any appreciable decrease in the concentration the total volume of circulating protein decreases and the reserve protein (for the existence of which they produced evidence) is largely used up.

10. Greenberg, D. M.: The Colorimetric Determination of Serum Proteins, J. Biol. Chem. **82**:545 (May) 1929.

sufficient to lead to any conclusion other than that the protein content of the serum is normal. This conclusion was supported by determining only the albumin content in about fifty cases (one would expect to find any important variations in the amount of albumin), the average value being 4.38 per cent for both men and women. In fact, the lowest amount of albumin obtained in 106 analyses of the blood of patients with epilepsy was 3.7 per cent, and the highest, 5.16 per cent. Neither value could be considered far from normal, if one accepts the ranges given by Peters and Van Slyke[11]: albumin, from 3.95 to 5.24 per cent, and globulin, from 1.56 to 2.98 per cent. These authors obtained the following average values for a large number of normal persons: albumin, 4.44 per cent, and globulin, 2.28 per cent. Our averages for the blood of both normal persons and those with epilepsy agree closely with these values as regards albumin content, but we have rather consistently found lower amounts of globulin in the blood of both types of subjects.

TABLE 1.—*Results of Studies of the Albumin and Globulin Contents of the Blood of Normal Persons and of Patients with Epilepsy*

Type of Case	Subjects Used as Controls	Patients with Epilepsy	
		Men	Women
Number of cases	10	14	15
Albumin, percentage			
High	4.92	4.83	4.71
Average	4.54	4.50	4.46
Low	4.35	4.15	3.88
Globulin, percentage			
High	1.97	2.56	2.43
Average	1.80	1.90	1.89
Low	1.54	1.49	1.63
Average albumin-globulin ratio	2.52	2.37	2.37

By studying each case represented in the averages shown in table 1 as a separate entity, we made an attempt to correlate the frequency of convulsions and the time since the last convulsion with the amount of serum protein, but no correlation seems to exist. Patients having an average value for the protein content of the serum are as likely to have frequent convulsions or to have had them recently as those for whom a low or a high protein content was shown.

It seemed to us worth while, however, to investigate the blood of patients with epilepsy as soon as possible (within a few minutes) after a convulsion and then to make observations for a day or two. Certainly then, if ever, significant changes should be observed. The results proved to be of interest because of their constancy.

In this series of analyses there seems to be a tendency toward lower values for globulin after the convulsion, but it is questionable whether

11. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, p. 662.

any importance should be attached to this observation. The results and the averages are all within the normal range, and in two cases notably (those of L. B. and J. C.) the protein content remained almost constant. One would seem justified, therefore, in concluding that there is no significant change in the albumin or globulin content at the time of or after a convulsion that could not be accounted for by experimental error.

TABLE 2.—*Values for the Albumin and Globulin Contents of the Blood of Patients with Epilepsy in Relation to the Recentness of Seizures*

	Content at Seizure, %		Content 10–12 Hours After Seizure, %		Content 24–36 Hours After Seizure, %	
Patient	Albumin	Globulin	Albumin	Globulin	Albumin	Globulin
F. H.	4.32	2.06	4.48	1.95	....	....
R. C.	4.54	2.30	4.46	1.91	....	....
B. K.	4.11	1.98	4.25	1.69	....	....
K. C.	4.32	2.36	4.76	2.20	....	....
D. O.	4.90	2.40	4.35	1.82	4.40	1.69
C. B.	4.39	2.07	4.29	1.76	....	....
J. C.	4.60	1.50	4.69	1.60	4.60	1.52
A. T.	4.58	1.80	4.67	1.67	5.16	1.90
L. B.	4.19	2.45	4.21	2.24	4.25	2.17
D. H.	4.90	2.51	4.69	2.07	4.31	1.83
Average	4.49	2.14	4.46	1.89	4.55	1.82
Average value of albumin-globulin ratio	2.1		2.36		2.5	

SUMMARY

The amount of serum protein has been determined for a large number of patients with epilepsy. The values for albumin and globulin are within the normal range and show essentially normal averages.

There is no apparent correlation between the values for serum protein and the frequency or recentness of convulsions.

The protein content of blood drawn immediately after a convulsion is normal, and the content remains normal when studies are made over a period of from twenty-four to thirty-six hours, although almost without exception there is a decrease in the amount of serum globulin after the convulsion.

CENTRAL LEVELS OF SENSORY INTEGRATION

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The spinal cord, at least in higher animals, almost exclusively plays the rôle of a conductor with regard to sensation. The thalamus and the cerebral cortex are the essential integrating sensory mechanisms, and it is with these two mechanisms that I shall deal.

Knowledge of the functions of the thalamus began in the middle of the nineteenth century with Luys, Todd and Carpenter, who conceived of the thalamus as the subcortical center to which the sensory pathways and impulses converge. This was established anatomically by von Monakow, and it is generally accepted today. I think that all the various impulses, segregated in the spinal cord, finally reunite in the thalamus. There the final, thalamocortical neurons begin, which end in the somatic sensory cortex.

Modern neurology of the thalamus dates from the clinical investigations of Dejerine, Long and Roussy and the experimental work of Roussy. These investigations established that destruction of the ventrolateral thalamic nuclei results in the well known thalamic syndrome: more or less marked hypesthesia and hypalgesia of the skin and profound impairment of the various forms of deep sensibility in the contralateral half of the body. Furthermore, spontaneous, paresthetic sensory disturbances, usually of a painful, unpleasant nature, are present. Finally, ataxic, choreatic or athetosic motor disturbances can be observed. Motor paralysis is not present in the pure thalamic syndrome. Only the sensory symptoms are of concern here.

Whereas the cutaneous hypesthesia and hypalgesia and the disturbances in deep sensibility are easily understood as the consequence of the destructive lesion of the ventrolateral nuclei, the typical, spontaneous sensory disturbances are less easily explainable. The earliest explanation was that they were due to central irritation. Head, dissatisfied with this view, tried to account for them by the hypothesis that the cortex normally inhibits the sensory thalamic nuclei and that their activity, especially that of the medial nuclei, freed from cortical control, exhibits itself in the painful, paresthetic disturbances. The medial nuclei, the "essential center" of the thalamus, are important in this respect, according to Head and Holmes, in that they control the "affec-

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Read at the Fifteenth Annual Meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 28, 1934.

tive" component in the various sensory perceptions. I confess that I have always felt some doubt about the plausibility of this hypothesis. If it were correct, one would expect similar disturbances to appear after lesions of the sensorimotor cortex with subsequent secondary degeneration of the ventrolateral thalamic nuclei. This, as is well known, is not the case.

Whatever the explanation of these peculiar paresthetic disturbances may be, the fact remains that Head and Holmes were the first to stress that the medial thalamic nuclei play a rôle in the elaboration and integration of the sensory impulses.

A few years ago Dr. O. Sager of Bucharest and I [1] applied the method of local strychninization to the study of the sensory functions of the thalamus in cats. The injection of a minute quantity (from 1 to 2 cu. mm.) of a 1 or 2 per cent solution of strychnine into the thalamus of the cat results in a typical complex of symptoms, exactly the same as that which appears on local application of strychnine to the sensory cortex: marked hypersensibility to various peripheral stimuli (touch, pain, temperature and deep stimuli) and also typical symptoms of spontaneous, paresthetic disturbances, presumably of a very disagreeable, unpleasant nature. These symptoms appear on strychninization of the ventral and lateral thalamic nuclei; the same symptoms occur on strychninization of the medial thalamic nuclei.

The fact that the symptomatology resulting from strychninization of the medial nuclei is the same as that caused by local strychnine poisoning of the ventrolateral nuclei must not be interpreted as indicating that the functions of these two nuclear groups with regard to sensation are the same. As has been pointed out on previous occasions, strychnine applied locally to central sensory mechanisms brings about the maximum of sensory functions, respects functional boundaries and does not produce functional caricatures. But this method has one limitation: In producing the maximum of sensory functions it blurs finer functional differentiations. For this reason the appearance of identical symptomatology after local strychninization of two sensory centers or two subdivisions of one center does not imply functional identity of the two (see also p. 773).

The sensory disturbances that occur on strychninization of one thalamus are present in the skin of both sides of the body but are strongest on the contralateral side. In the deeper structures they are present only on the contralateral side. This is true even after extirpation of the cortex of both hemispheres in the "acute" experiment and

1. Dusser de Barenne, J. G., and Sager, O.: Ueber die sensiblen Funktionen des Thalamus opticus der Katze, Ztschr. f. d. ges. Neurol. u. Psychiat. **133**:231, 1931.

after extirpation of one hemisphere in the "chronic" experiment and removal of the cortex of the other hemisphere in the "acute" experiment. In the latter preparation the ventrolateral thalamic nuclei of the first hemisphere have undergone secondary degeneration. Yet strychninization of the other thalamus produces the typical bilateral cutaneous sensory disturbances and the contralateral disturbances in deep sensibility. These facts show that the skin of both halves of the body and the deep structures of the contralateral half of the body are sensorially represented in each thalamus. This conclusion readily accounts, I think, for the clinical observation that in the thalamic syndrome the disturbances in cutaneous sensibility are often present for only a short time and diminish rapidly, whereas the impairment of deep sensibility is more marked, invariably of longer standing and often permanent.

(It may be pointed out here that many years ago Probst demonstrated fibers of the medial lemniscus crossing the midline to enter into the opposite thalamus.)

These experiments with Sager established another fact, namely, the existence of functional localization in the thalamus. One finds there a face, an arm and a leg area. But in contrast with the subdivision of the sensory cortex, these thalamic areas for the three portions of the body are not sharply separated. On the contrary, they are rather widely overlapping (fig. 1). This expresses itself in the fact that usually the sensory disturbances are localized not only in the face or the arms or the legs, but in the face and the arms or in the arms and the legs, and sometimes even are present in all parts of the body. Only on strychninization of the most ventral portion of the ventral nucleus does one find the disturbances exclusively in the face, whereas the hindleg seems to be represented separately in the dorsal portion of the lateral nucleus. This overlapping of the various thalamic areas expresses itself also in the fact that sensory irradiation from the arms to the face and from the face to the arms has been observed in these experiments.

Of importance for an understanding of the thalamic functions is the observation that the symptomatology on strychninization of the thalamus, at least in the cat, is the same after extirpation of the cortex of both hemispheres, even in the "acute" experiment, for it indicates the high level of functional integration attained in the thalamic activity of the cat with regard to sensation.

I come now to the cortical sensory level.

As is well known, the problem of the cortical representation of sensibility has been hotly debated since 1870, the memorable year of the discoveries of Fritsch and Hitzig. Older neurophysiologists—Munk, Ferrier, Luciani, Schafer, Horsley and many others—taught, although on inconclusive evidence, that the motor cortex was also endowed with sensory functions and was thus a true sensorimotor cor-

tex. Then came the reaction with the experiments of Sherrington and his collaborators. Sherrington gave full evidence of the fact already shown by Hitzig (1874) that the cortex, which in monkeys and primates yields primarily motor responses on electrical stimulation, lies in the precentral gyrus. This was generally interpreted as indicating that in these higher animals the motor region occupies a separate position on the cerebral cortex from that occupied by the sensory region, although

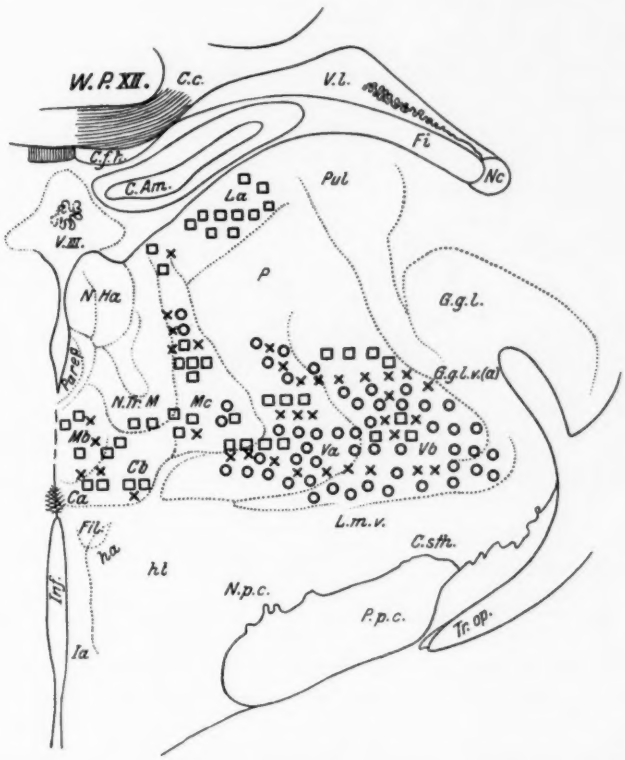

Fig. 1.—Frontal section through the thalamus at the level of plate XII of the atlas of the cat's brain of Winkler and Potter. The squares mark the localization of the hindlegs; the crosses represent that of the front legs, and the circles give the localization of the head in the thalamus. *C.c.* indicates corpus callosum; *Fi,* fimbria; *Nc,* nucleus caudatus; *C.Am.,* cornu ammonis; *La,* nucleus lateralis anterior; *Pul,* pulvinar; *Va* and *Vb,* nucleus ventralis; *N Ha,* nucleus habenulae; *Mb* and *Mc,* nucleus medialis; *Parep,* nucleus parependymalis; *N.Tr.M,* nucleus tractus Meynert; *L.m.v.,* lamina medullaris ventralis; *C.sth.,* corpus subthalamicum; *P.p.c.,* pes pedunculi cerebri, and *Tr.op.,* tractus opticus.

obviously this conclusion is not warranted. But this conception received additional support from experimental and clinical evidence which showed that large lesions of the postcentral gyrus are accompanied by sensory

disturbances, whereas lesions of the precentral cortex do not give rise to appreciable sensory defects, at least not to sensory impairment detectable with the ordinary methods of clinical investigation.

When the method of local strychninization was applied to the problem of functional localization of sensation in the cortex, it became evident that the physiologists and neurologists who proclaimed the existence of a sensorimotor region in the cerebral cortex were right.

The sensory area of the cerebral cortex, as revealed by the strychnine method, in the monkey occupies a large area on the precentral and on the postcentral cortex (fig 2).

The symptomatology in these experiments on the cortex is the same as that found in the later experiments on the thalamus: typical paresthetic disturbances, hyperesthesia and hyperalgesia. The disturbances

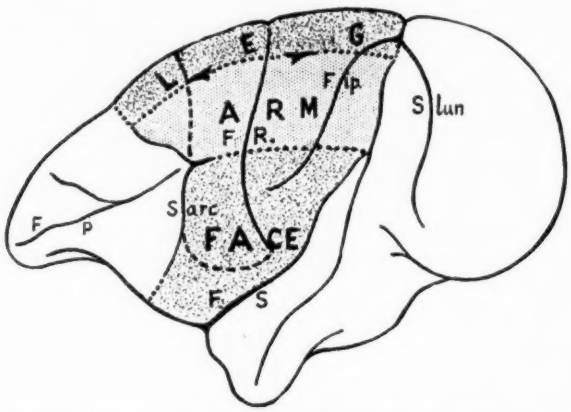

Fig. 2.—Sensory cortex on the convexity of the hemisphere in Macacus as revealed by the method of local strychninization (Dusser de Barenne, 1924). The dotted lines indicate the boundaries between the three subdivisions of the sensory zone; and the broken line, the frontal boundary of the electrically excitable cortex. Between the leg and arm areas probably lies the trunk area. *F R* indicates the fissura centralis; *F S*, the fissura sylvii; *F ip*, the fissura interparietalis; *S lun*, the sulcus lunatus; *S arc*, the sulcus arcuatus, and *F P*, the fissura principalis.

on strychninization of a few square millimeters of this area of one hemisphere are present, so far as the skin is concerned, in both halves of the body. They are strongest on the contralateral side, but are also markedly present on the homolateral side. Disturbances in deep sensibility (hypersensitivity to pressure of the deeper structures) are usually found only in the contralateral half of the body. It can be shown that the skin of both sides of the body is represented sensorially in the sensory cortex of one hemisphere or, in other words, that the skin of one half of the body is represented sensorially in both hemispheres.

It is of interest to note here that Foerster observed the occurrence of bilateral paresthetic disturbances on electrical stimulation of the upper parietal gyrus in man (fields 5 α and 5 β of Brodmann) and in cases of irritative processes located in this region of the cortex.

The symptomatology of acute destructive lesions of the sensory cortex in man is in agreement with the findings in these experiments of cortical strychninization. Initially, marked hypesthesia and hypalgesia of the skin and abolition of deep sensibility exist. In cleancut cortical lesions, especially after surgical extirpations, the cutaneous sensory disturbances rapidly subside to a great extent, often almost completely; loss of spatial localization and discrimination are permanent symptoms. Impairment of the various modalities of deep sensibility remains observable much longer and is often permanent. It is worth while to point out that in the clinical lesions and in these experiments with strychnine the symptoms of deficit in the former group and the symptoms of sensory excitation in the latter are present predominantly in the apical parts of the body, i. e., in the hands and forearms or in the feet and legs.

These experiments on the cortex reveal a sharp subdivision of this large sensory zone into three major portions: (1) a face area, (2) an arm area and (3) a leg area. Between the arm and the leg area probably lies (4) a trunk area. Sharp functional boundaries seem to exist between these various subdivisions; they are respected even by strychnine. Sensory irradiation has never been observed in these experiments on the cortex.

Local strychninization of portions of the precentral sensory cortex and of the postcentral cortex results in the same symptomatology. As all experimental and clinical evidence indicates that the sensory functions of the precentral cortex must be different from those of the postcentral cortex, this similarity in the symptomatology on strychninization of the precentral and postcentral cortex can be interpreted only as demonstrating that strychnine, in bringing about the maximum of sensory functions, blurs finer functional differentiations. This is the limitation of this method, to which I have referred in discussing the experiments on the thalamus with strychnine (p. 769).

One of the facts in these experiments on the cortex that has always been most amazing to me is that strychninization of only a few square millimeters of any of the large subdivisions of the sensory cortex of the monkey suffices to produce the typical symptomatology in the cutaneous sensibility of both arms.

Two explanations of this seem to present themselves: The first is that in those few square millimeters of cortex the skin of both arms is represented sensorially. A priori this conception is highly improbable; its incongruity is evident if one realizes that this explanation would

imply at least a hundredfold, if not two hundredfold, representation of this large body surface in the precentral and postcentral sensory arm areas. The second possible explanation, which I have always defended, is that strychninization of the few square millimeters of cortex of the sensory arm area sets on fire the cortex of the whole sensory arm area and furthermore those portions of the optic thalamus in which the sensibility of the arms is represented.

The second of these assumptions seems necessary to explain the appearance of the complete, typical symptomatology on strychninization of a few square millimeters of one precentral arm area, the rest of which has been procainized, while the entire homolateral, postcentral and contralateral precentral and postcentral arm areas have been extirpated (fig. 3).

This conception of a close functional correlation between the thalamus and the cortex was given long ago by Head and Holmes, Wallen-

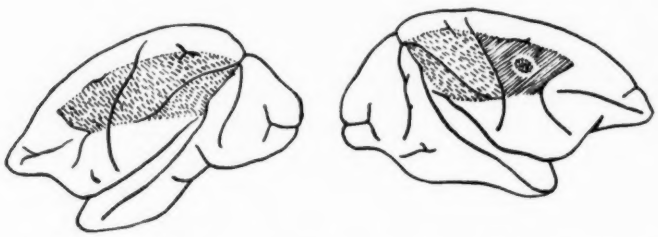

Fig. 3.—Diagram showing extirpation of the whole sensory arm area of the left hemisphere and of the postcentral and parietal sensory arm areas of the right hemisphere, with procainization of the precentral sensory arm area of this hemisphere, except for a small region which was strychninized locally in the usual manner. The diagonal lines indicate the procainized area; the broken lines, the extirpated area, and the dots, the strychninized area.

berg and others. Furthermore, this conception is in harmony with the existence of the large number of corticothalamic fibers, which have been known for many years (by von Monakow, Dejerine and others). Recent anatomic investigations (by Poljak and others) have again emphasized this mutual anatomic relation between the thalamus and the sensory cortex. One cannot escape, in my opinion, the assumption of a very close interaction between these two levels of the nervous system in sensation. The functional level of thalamic sensory integration is a very high one, and the cortex, operating in intimate mutual relationship with the thalamus, furnishes the ultimate differentiation within sensation.

Figure 4 represents diagrammatically some of the more important connections of the thalamus and cortex as they can be laid down at

present, partly on the basis of the results of the experiments with the strychnine method.

The neurons represented by the cells *a* and *b* and the fibers *3* and *4* represent the well known thalamocortical neurons originating in the ventrolateral nuclei, which undergo retrograde degeneration after extirpation of the cerebral cortex. In these nuclei end many corticothalamic neurons (*g 5* and *h 6*). As the symptomatology on strychninization of the medial thalamic nuclei (in the cat) is the same before and after extirpation of the cortex, it follows that the medial nuclei must receive afferent impulses from the periphery through afferent fibers

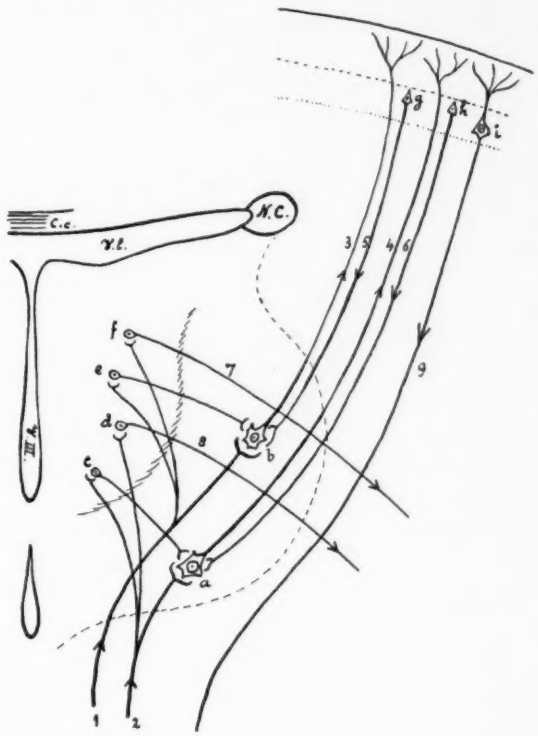

Fig. 4.—Some of the more important connections of the thalamus and cortex, based partly on the results of experiments with the method of local strychninization: *a* and *b* are cells of the ventrolateral thalamic nuclei, from which originate the thalamocortical axons *3* and *4*; *c*, *d*, *e* and *f* are nerve cells of the medial thalamic nuclei; *c* and *e* send their impulses to cells *a* and *b* of the ventral nuclei; *d* and *f* discharge their impulses along axons *7* and *8* to subcortical, extrapyramidal motor mechanisms. The cells of the ventrolateral nuclei, as well as those of the medial thalamic nuclei, receive afferent impulses from subcortical levels through axons *1* and *2* of the medial fillet; *g* and *h* are cells of the cerebral cortex giving rise to axons *5* and *6*, which innervate cells *a* and *b* of the ventral thalamic nuclei; *i* is a giant pyramidal cell of the cortex from which originates axon *9*, a fiber of the corticospinal tract; *C.c.* indicates corpus callosum; *N.C.*, nucleus caudatus; *V.l.*, ventriculus lateralis, and *V.III.*, ventriculus tertius.

(*1* and *2*). For simplicity these connections are represented by collaterals from fibers *1* and *2* ending around the cells *c, d, e* and *f* of the medial nuclei. That marked symptoms of sensory excitation occur after local strychinization of the medial thalamic nuclei after extirpation of the cortex indicates that the afferent impulses transmitted to these cells of the medial nuclei must be able to act on efferent, extrapyramidal mechanisms. This conclusion is expressed in figure 4 by the neurons *d 8* and *f 7*. Possibly neurons originating in the medial nuclei can influence also the neurons of the ventrolateral nuclei (*a 4* and *b 3*). Neuron *i 9* is a corticofugal, pyramidal neuron.

The conception given offers, I think, a plausible explanation for many experimental and clinical observations. Among these I wish to emphasize one, namely, the remarkable regression of sensory impairment, especially of the cutaneous symptoms of deficit, after cortical lesions. Three reasons can be given why this regression, this functional recovery of sensation, occurs: The first is that the sensory region of the cerebral cortex is much larger than was formerly supposed; the second is that the skin of both halves of the body is represented in the sensory region of one hemisphere or, in other words, that each half of the body surface is sensorially represented in both hemispheres. In agreement with the unilateral representation of deep sensibility is the observation that its disturbances show only partial recovery, much less than those of cutaneous sensibility. The third reason is that the functional level of thalamic sensory integration is a very high one. This has been shown experimentally for the cat's brain. I hope to be able to show this also for the monkey's brain in the near future.

I am fully aware that the picture which I have drawn here is a rough one, but in the present state of knowledge only a sketch, a general outline, seems possible. I can only hope that even as such it is not entirely inadequate.

SPECIAL ARTICLES

NEUROGENIC VESICAL DYSFUNCTION

ALTERATIONS IN THE PHYSIOLOGY OF MICTURITION DUE TO LESIONS OF THE NERVOUS SYSTEM

C. D. CREEVY, M.D.
MINNEAPOLIS

Disturbances in micturition due to diseases of the nervous system have long been known to occur with considerable frequency, and various phases of their relationship have been the subject of much careful study. However, most of the literature deals with some isolated aspect of the problem, such as the peripheral innervation of the bladder, the cystoscopic findings in nervous disorders and the treatment of certain forms of disturbances of the bladder due to nerve lesions. In some of these fields knowledge is relatively exact and is sufficient for practical purposes; in others, it is inexact or controversial. Confusion has been fostered by the tendency, of urologists especially, to attach to the condition of disturbed function of the bladder due to nervous disease several ambiguous terms such as cord, neurogenic and neurogenous bladder. The recently suggested term neurogenic vesical dysfunction (Smith and Engel [1]) is preferable because it is precise and descriptive and implies a pathologic state, an implication which is lacking from the other names.

This paper is an attempt to classify and to correlate existing knowledge bearing on the relation between disturbed function of the bladder and disease of the nervous system, particularly from the point of view of diagnosis and treatment, and is based on existing literature.

ANATOMY OF THE BLADDER

The urinary bladder is a saclike structure formed of three irregularly interwoven layers of smooth muscle (detrusor urinae) and lined by transitional epithelium separated from that muscle everywhere except over the trigon by loose vascular submucosa. The trigon is a triangular sheet of smooth muscle formed by the interdigitation of the longitudinal muscle layers of the ureters. It rests on the inner surface of the muscle coat of the base of the bladder, to which it is adherent, and is inserted

From the Division of Urology of the Department of Surgery, the University of Minnesota Medical School.

1. Smith, C. K., and Engel, L. P.: Neurogenic Vesical Dysfunction in Children, J. Urol. **28**:675, 1932.

along the anterior surface of the posterior wall of the prostatic urethra. The overlying mucosa is intimately attached to the muscle of the trigon.

Some difference of opinion exists as to the internal vesical sphincter. According to Morris,[2] it is a ringlike thickening of the detrusor urinae which surrounds the internal urinary meatus. Young and Wesson[3] described it as two loops of unstriated muscle, one from the external and one from the internal muscular layer of the bladder, which arise posterior and lateral to the internal urinary meatus and sweep forward around the prostatic urethra (fig. 1 *A*). Others doubt whether an internal sphincter exists as such but regard it as merely an opening in the detrusor urinae, the tone of which exercises a sphincteric action.

The external sphincter lies between the layers of the urogenital diaphragm and consists of two striated muscles, the sphincter urogenitalis

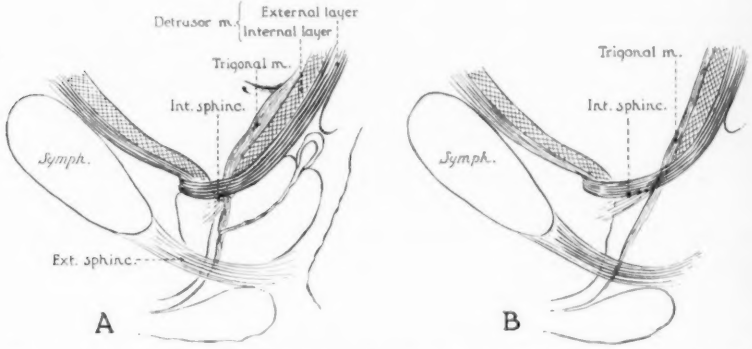

Fig. 1.—*A*, the vesical sphincters (after Young and Wesson[3]). *B*, the rôle of the trigon in opening the internal sphincter.

urethrae and the transversus perinei profundus; so far as is known, they act as one muscle.

INNERVATION OF THE BLADDER[4]

Peripheral Nerves and Ganglia.—Information on this subject is abundant, and agreement on the anatomic facts is general. There is still a good deal of disagreement about the function of the various nerves.

2. Morris, H.: Human Anatomy, edited by C. M. Jackson, Philadelphia, P. Blakiston's Son & Co., 1921, pp. 475 and 1283.

3. Young, H. H., and Wesson, M. B.: The Anatomy and Surgery of the Trigone, Arch. Surg. **3**:1 (July) 1921.

4. References to most of the literature on the vesical innervation will be found in the following papers: Gruber, C. M.: The Autonomic Innervation of the Genito-Urinary System, Physiol. Rev. **13**:497, 1933. Lichtenstern, R., and Marburg, O.: Ueber initiale Störungen bei organischen Nervenkrankheiten, Ztschr. f. urol. Chir. **38**:145, 1933.

The bladder and its sphincters derive their nerve supply from three main sources, namely, the pudic (pudendal), the pelvic (nervus erigens) and the hypogastric (presacral) nerves, all of which contain both afferent and efferent fibers.

The pudic nerve derives its motor fibers from the anterior, and its sensory fibers from the posterior, roots of the first three or four sacral segments of the spinal cord. It carries sensory impulses from the urethra and motor impulses for contraction of the external sphincter (voluntary muscle).

The pelvic nerve, a part of the parasympathetic nervous system, is also derived from the first three or four sacral segments of the spinal cord. It conveys most of the sensory impulses from the wall of the bladder and bears motor impulses to it through the parasympathetic ganglia in the vesical plexus. Many of the older observers believed that it also carried inhibitory impulses which relaxed the internal sphincter, but this is not generally conceded. The cystoscopic observations of Young [5] and the anatomic studies of Young and Wesson [3] make it seem more plausible that it carries motor impulses to the trigonal muscle and thus on stimulation causes contraction of the detrusor muscle and at the same time pulls the internal sphincter open (fig. 1 *B*); however, since it responds by contraction to sympatheticomimetic drugs, it may be supplied by the hypogastric nerve.

The hypogastric nerve or plexus (presacral nerve) is a part of the sympathetic nervous system. Its motor fibers are derived from the second to the fifth lumbar segment of the spinal cord; they follow the white rami communicantes to the abdominal sympathetic trunk, then traverse the gray rami to reach the inferior mesenteric ganglion, where most have synapses; their postganglionic fibers form the lower ganglia of the abdominal sympathetic trunk as well as a few preganglionic fibers from the aortic plexus. The latter have their synapses in the ganglia of the wall of the bladder.

About 25 per cent of the fibers of the hypogastric plexus carry vesical sensation. These enter the spinal cord as high as the middle thoracic segments.

Nine or more separate functions have been ascribed to the hypogastric nerve: inhibition of the detrusor muscle; contraction of the ureteral meatus, trigon, internal sphincter and smooth muscle of the prostate and seminal vesicles; transmission of a sense of distention of the bladder and spasm, and vasomotor impulses to the bladder. Some investigators have also noted contraction of the detrusor muscle on hypogastric stimulation.

5. Young, H. H.: Practise of Urology, Philadelphia, W. B. Saunders Company, 1926, vol. 1, p. 4.

Of these functions, inhibition of contraction of the detrusor muscle has been most emphasized and has led to the designation, "nerves of bladder filling." McCrea and Macdonald [6] attributed the divergent experimental results which have produced the conflict of opinion to the use of different species of animals, to differences in the tone of the bladder at the beginning of experiments and to the effect of the anesthetics employed in the experiments. Ultimately it should be possible to draw conclusions on these points if the results of the many presacral neurectomies now being performed are some day tabulated.

Connections of the Nerves of the Bladder.—Peripheral: While the nature and functions of the peripheral nerves of the bladder are fairly well understood, their central connections are much less clear.

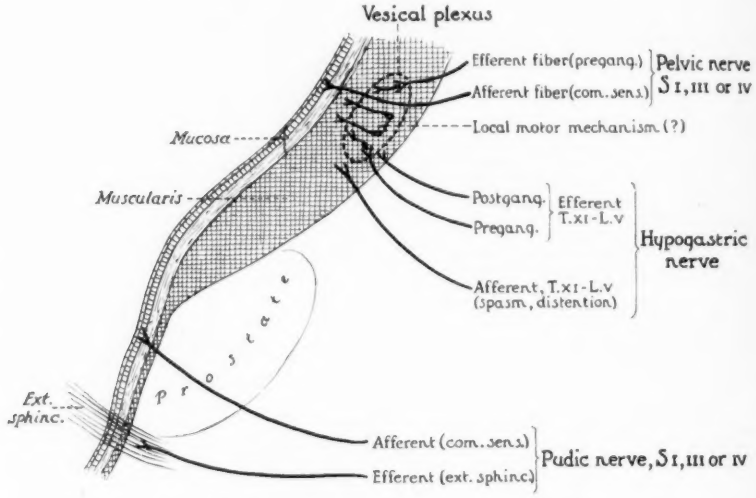

Fig. 2.—Peripheral innervation of the bladder.

It is believed by many investigators that the vesical plexus with its ganglion cells contains a local mechanism (fig. 2) which can produce contraction of the bladder even though it is separated entirely from the central nervous system; they attribute the reflex or automatic micturition seen in cases of complete severance of the spinal cord to its influence. It is not unlikely that this contractility is myogenic and thus is independent of the nervous system.

Central: Others hold that there are reflex centers in both the lumbar and the sacral segments of the cord; as evidence for this view it is alleged that lesions which destroy the sacral segments produce a dis-

6. McCrea, E. O., and Macdonald, A. D.: Presacral Sympathectomy and the Urinary Bladder, Brit. J. Urol. **20**:267, 1928.

turbance of micturition differing in character from that which is due to lesions of the cord at a higher level, that is, that destruction of the sacral portion of the spinal cord produces a flaccid bladder with flaccid sphincters from which urine dribbles continuously from the beginning and that a transverse lesion above the first sacral segment leads at first to complete retention with spastic sphincters. Other observers, however, have stated that the level of the lesion is without influence on the type of disturbance of the bladder except that, if it is below the middorsal level, distention of the bladder can still be felt (hypogastric sensory fibers).

The course of the afferent fibers from the bladder, once they have reached the posterior spinal roots of the sacral and lumbar segments, is not definitely known, but it is assumed to lie in the posterior columns since tabes dorsalis, which involves this area, produces hypesthesia or anesthesia of the bladder.

Uncertainty also prevails as to the course of the vesical efferent nerves, although it seems most probable that they lie in or about the crossed pyramidal tracts; Barrington [7] located them in the dorsal half of the lateral column in the cat.

There are many theories as to the location of the numerous centers for micturition which have been postulated in various parts of the brain, but definite conclusions have been prevented by several circumstances: 1. The bilaterally symmetrical character of the brain is such that lesions, to affect the function of the bladder, must also be bilaterally symmetrical, or their effects are transient. 2. There appear to be centers capable of carrying out automatic micturition which are located both in the spinal cord and in the vesical plexus; their existence makes evaluation of the rôle of the brain in micturition most difficult. 3. Motor and sensory centers and tracts lie in such close apposition that the common focal lesions usually affect at least two of the three. 4. Sherrington [8] stated that it is not possible to influence the tone or contraction of the bladder by stimulating any area in the cerebral cortex.

Nevertheless, at least six cerebral centers or groups of centers for micturition have been described, namely: (1) the detrusor voluntary center; (2) one for the internal sphincter; (3) one for the external sphincter; (4) several subcortical motor centers; (5) one or more nuclei for coordination or correlation, and (6) one or more sensory centers.

A center for contraction of the detrusor muscle is generally said to exist in the precentral gyrus near that for the hip muscles (in the

7. Barrington, F. J. F.: The Effect of Lesions of the Hind and Midbrain on Micturition in the Cat, Quart. J. Exper. Physiol. **16**:81, 1925; The Component Reflexes of Micturition in the Cat, Brain **54**:177, 1931.

8. Sherrington, C. S.: The Lumbosacral Plexus, J. Physiol. **13**:678, 1892.

inner part of the sigmoid gyrus in the cat). A center for the internal sphincter has been described in the paracentral lobule as well as in the outer part of the sigmoid gyrus. If, as has already been suggested, the internal sphincter plays a passive rôle in micturition, being pulled open by the trigonal muscle and closed by its own inherent tone, such a center probably presides over the tone of the sphincter without causing it to relax or contract actively. The center for the external sphincter is said to be located in the precentral gyrus.

It has been found by various investigators that stimulation of certain subcortical areas evokes contraction of the bladder, and several have suggested that centers exist here (cerebral peduncles, thalamus, corpus striatum), but one wonders whether these workers have merely stimulated the cut ends of efferent tracts issuing from the centers in the cerebral cortex itself or whether the stimulus spread to adjacent efferent fibers. To these subcortical centers has been attributed the function of carrying out acts which are initiated wilfully but executed automatically, which is a rather fine distinction from a purely voluntary act.

To several areas have been assigned rôles in correlating and coordinating the various parts of the nervous system involved in micturition. These have been variously located in the frontal lobe, in the cerebellum and in the corpus striatum. Their existence cannot be said to have been proved.

The centers for perception of fulness of the bladder and pain have been assigned to the gyrus fornicatus and to the midbrain. Barrington's experiments strongly suggest that the latter view is correct.

THE FUNCTION OF THE BLADDER

In order to explain clearly the manner of function of the bladder it is easiest to follow the normal sequence of events, beginning with the viscus empty. In this state the sphincters are closed by their inherent tone, and the detrusor muscle is similarly in a state of tone, so that the cavity of the bladder is obliterated, as may be verified by passing a catheter immediately after urination, when in ordinary circumstances only a drop or two of urine will be recovered. Since secretion of the urine is normally almost continuous, filling begins at once but progresses slowly. As soon as a measurable quantity of urine is present in the bladder a pressure of from 6 to 10 cm. of water develops and is maintained in a remarkably constant fashion until a considerable volume of urine accumulates. Sherrington [8] has designated the ability of the viscus to relax as it fills and so to maintain a constant pressure as "postural tone." Watkins [9] has recently opposed this view, describing

9. Watkins, K. H.: The Clinical Value of Bladder Pressure Estimations, Brit. J. Urol. **6**:104, 1934.

a slow, progressive rise of pressure with filling. The fact that he injected relatively large quantities of fluid at a time vitiates the value of his results, since he did not simulate natural filling of the bladder.

The relaxation necessary for filling probably depends on impulses which travel via the sensory fibers of the pelvic or of the hypogastric nerve to the lumbar segments of the cord, where the cells of the sympathetic system are stimulated and send inhibitory impulses to the detrusor muscle by way of the hypogastric plexus (or nerve). It is, however, possible that the ability to relax is an inherent property of the muscle of the bladder and is in no way related to the nervous system, since relaxation on filling persists after division of any or all of the nerves of the bladder, excision of the vesical plexus and division or excision of the spinal cord. It is possible that the central nervous system and the hypogastric nerve cause relaxation of the detrusor muscle only when a conscious attempt is made to suppress the desire to void.

The point at which the balance between the volume of the contents of the bladder and its pressure is disturbed varies somewhat with external conditions since the intravesical pressure is influenced by such things as psychic stimuli (sounds and odors), by the temperature of the air and by changes in posture and activity (standing erect, coughing, laughing, straining), all of which may increase the tension within the bladder. In the absence of such factors the pressure of the bladder begins to rise when the volume of the contained urine approximates from 200 to 400 cc.; when the tension reaches from 18 to 30 cm. of water the subject becomes conscious of a desire to micturate.

At about this same pressure mild rhythmic contractions of the detrusor muscle appear. It is not certain whether these represent the inherent irritability of the detrusor muscle, i. e., are myogenic, or whether they involve the vesical ganglia or reflex centers in the spinal cord. It was originally thought that these contractions forced a few drops of urine into the prostatic urethra and produced the desire to void. This has been disproved by roentgen studies which have shown that the prostatic urethra is empty until the instant that micturition begins.

Up to this point there is little room for doubt as to the mechanism of function of the bladder, but as to the subsequent course of events there are still some disagreement and confusion. When the desire to void appears, either of two sequences may develop, depending on whether or not it is convenient to urinate.

If it is not, the external sphincter is voluntarily contracted, presumably by stimulation of its center in the cerebral cortex via association paths connecting it with the sensory center; closure of the internal sphincter is maintained by its tone. As is well known, the desire may then disappear for a time, probably by reason of a spinal reflex or a conscious effort involving inhibitory impulses via the hypogastric nerves.

On the other hand, the desire to void may become imperative, which indicates, as Rose [10] has shown, the existence of a high intravesical pressure resulting from contraction of the detrusor muscle. In this situation it is probably only necessary to relax the external sphincter or even to refrain from contracting it voluntarily, when the contraction of the detrusor and trigon already present will empty the bladder. This is based on the assumption that Young's theory of the function of the trigon is correct: that it pulls the internal sphincter open (Zuckerkandl [11] assigned the same rôle to a prolongation of the fibers of the detrusor muscle into the urethra).

The mechanism is somewhat different when a normal desire to urinate exists and circumstances permit emptying of the bladder. Here, the pressure of the bladder, being only from 18 to 30 cm. of water, is insufficient to bring about emptying of the bladder. The precise manner in which the pressure is now elevated, that is, detrusor contraction brought about, is not clear. It was, and still is, widely held that this is accomplished by the motor center for micturition in the cerebral cortex. It also seems probable that contraction may be brought about by a slight tightening of the abdominal muscles which in turn elevates the pressure of the bladder sufficiently to stimulate a local detrusor (and trigonal) contraction. Whether this secondary rise of pressure is accomplished by the action of the vesical ganglia, whether it involves a reflex arc in the spinal cord or whether it is due to the irritability of smooth muscle is not known. There are experimental data to indicate that the local mechanism may suffice, and in the person with complete destruction of the lower end of the spinal cord this local mechanism undoubtedly develops after a time, although never so completely as to cause complete emptying of the bladder. In all probability the resultant pressure is sufficient to overcome the tone of the external sphincter.

When no sensation of desire to void is present but the person wishes to initiate micturition for reasons of convenience I am certain that pressure of the bladder is elevated and detrusor-trigonal contraction instituted with the aid of the abdominal muscles and diaphragm and that the rôle of the external sphincter is passive here as well.

In concluding, certain accessory mechanisms involved in micturition should be mentioned. Thomsen [12] has emphasized the importance of an angulation of the midportion of the female urethra as a mechanical aid

10. Rose, D. K., and Rollins, R. R.: Pylonephritis in Pregnancy, J. A. M. A. **96**:235 (Jan. 21) 1931.

11. Zuckerkandl, O., in Eulenberg, A.: Real-Encyclopädie der gesamten Heilkunde, ed. 3, Vienna, Urban & Schwarzenberg, 1894, vol. 3, p. 331.

12. Thomsen, E.: Studies of the Female Urethra, Especially as Regards the Closing Mechanism of the Bladder, Acta radiol. **13**:433, 1932.

in maintaining its closure and has demonstrated that restoration of this angle restores control to incontinent women. Others believe that the levator ani elevates the prostatic urethra during micturition.

DISTURBANCES OF INNERVATION

Classification.—It is natural in studying the disturbance of function of the bladder due to nerve lesions to attempt a functional classification depending on whether the disorder is motor or sensory, destructive or irritative. Such a classification would be ideal were it not that all the peripheral nerves of the bladder are mixed and that the tracts and centers in the spinal cord which convey impulses of the bladder are so close together that many of the common lesions produce both sensory and motor disorders. The same holds true in the brain.

It would seem logical to speak of irritative or destructive lesions of the nerves to the detrusor muscle or sphincters until one considers that the peripheral nerves and the vesical plexus are mixed in function and that their tracts and centers are so closely connected that it is difficult to conceive of a lesion of the nervous system so small that it would involve, say, the external sphincter and spare the internal sphincter and detrusor muscle.

It is therefore necessary to be content with a loose, rather inaccurate classification which depends on the location of the lesion and on its nature.

If the hypothesis of function of the bladder already presented, namely, that it consists of a semiautomatic local process controlled and modified indirectly by the will, is correct it is plain, as Curling [13] pointed out in 1833, that lesions which disturb sensation are of the greatest importance, since voluntary control depends on an intact sensory apparatus; for even though the central portion of the motor apparatus is damaged, an intact local mechanism can be schooled to cause emptying of the bladder, but this local mechanism can ordinarily be controlled only if some slight sensation is present. It is, of course, theoretically possible to bring about urination by training even in the entire absence of sensation, but the lack of coordination (ataxia) which this would produce makes it doubtful if it could be achieved satisfactorily.

The importance of sensation to normal function of the bladder is emphasized by the observation of Shattock [14] that cocainization of the mucosa of the cat's bladder causes temporary retention and overflow; Curling [13] and Smith and Engel [1] found that section of the sacral

13. Curling, H. B.: Affections of the Urinary Bladder in Paraplegia, London M. Gaz. **13**:353, 1833.

14. Shattock, S. G.: Is There an Idiopathic Dilatation of the Urinary Bladder? Proc. Roy. Soc. Med. (Sect. Path.) **2**:88, 1908.

posterior roots also caused retention and overflow and Barrington[7] noted that residual urine always occurred with complete loss of sensation. Von Frankl-Hochwart[15] said that he had never seen a lesion of the bladder nerve supply involving only its motor portion; nevertheless, such lesions probably occur in diseases like polyomyelitis and amyotrophic lateral sclerosis.

Experimental Production of Lesions.—The effects of lesions of the peripheral nerves have been thoroughly investigated in the dog and cat and may be summarized as follows: Section of the hypogastric nerves produces only a slight, transitory increase in the frequency of micturition which soon disappears, a fact which suggests that the ability of the bladder to relax as it fills, while perhaps normally dependent on the hypogastric nerves, may at times depend on some local mechanism (myogenic?). Section of the pudic nerve at first results in some prolapse of the urethral and rectal mucosa during micturition and in a little urinary incontinence, variously attributed to paralysis of the external sphincter and to anesthesia of the urethra. As the disturbances soon disappear, it seems that anesthesia is the more probable cause, since the sensory fields of both the pelvic and the hypogastric nerve overlap that of the pudic; but it is difficult to explain either nerve taking over a motor function so opposed to its usual one. It is this evidence, together with that of Rehfisch[16] and Young[5] already mentioned, which suggests that urinary continence is due to the tone rather than to the active contraction of the sphincters.

Division of the pelvic nerves has more far-reaching effects. The bladder becomes distended and then overflows; periodic voiding and a sense of fulness of the bladder are lost. After a variable interval periodic micturition develops but is involuntary and incomplete, although the volume of residual urine may ultimately become quite small. Some writers have stated that sensation returns; others have denied it.

Division of the hypogastric in addition to the pelvic nerve produces no change; cutting the pudic and pelvic nerves produces at first true incontinence with continuous dribbling and an empty bladder, but periodic involuntary incomplete urination soon returns. The same thing happens even after division of all the nerves of the bladder or removal of part of the thoracic and all the lumbosacral portion of the spinal cord.

These facts may be taken as incontrovertible evidence that there exists a local mechanism capable of causing contraction of the bladder

15. von Frankl-Hochwart, L.: Ueber Harnretention ohne Lokalhindernis, Wien. med. Wchnschr. **57**:2194, 1907; **58**:2188, 1908. von Frankl-Hochwart, L., and Fröhlich, A.: Ueber die corticale Innervation der Harnblase, Neurol. Zentralbl. **23**:646, 1904.

16. Rehfisch, E.: Ueber den Mechanismus des Harnblasenverschlusses und der Harnentleerung, Virchows Arch. f. path. Anat. **150**:111, 1897.

without the intermediation of the central nervous system—a fact of considerable importance clinically.

To determine whether this mechanism is nervous or muscular the ganglia have been removed from the wall of the bladder; it remained irritable. It cannot be determined, however, whether the subsequent failure of periodic micturition to return was due to removal of the ganglia or to coincident damage to the wall of the bladder and to its blood supply.

Considerable study has been devoted to the effects of lesions of the spinal cord on function of the bladder. It has been demonstrated that destruction of the cauda equina produces true incontinence. There is a division of opinion as to whether periodic micturition later develops. Transverse lesions above the cauda equina cause retention, then overflow, then periodic incomplete involuntary micturition.

The most illuminating experimental studies of the results of lesions of the brain have been made by Barrington,[7] who found that decerebrate cats could urinate, that bilateral destruction of a small area ventral to the superior cerebellar peduncle produced residual urine regularly and that destruction of the midbrain from the ventral half of the side of the posterior end of the aqueduct to beyond the mesencephalic root of the fifth nerve abolished periodic micturition.

Most of the other work on which knowledge of cerebral centers is based consists either of experiments on stimulation or of autopsy studies of the brains of patients whose micturition was disturbed. This last material is limited in value by the fact that most of the lesions found post mortem have been too large to permit accurate conclusions.

The Symptoms of Neurogenic Vesical Dysfunction.—These are numerous and often confusing, a fact easily understood in view of the data previously noted. It may be taken as axiomatic that the neurologic diagnosis cannot usually be determined with precision from the urinary symptoms or cystoscopic or cystometric findings but depends on careful neurologic examination. This is true because certain lesions of the peripheral nerves may produce alterations of function of the bladder indistinguishable from those caused by disease of the spinal cord or cerebral disease, while two or more diseases of the spinal cord may produce identical disturbances in the bladder.

Any type of disturbance of micturition may be produced by lesions of the nervous system. For the sake of clarity these will be taken up in an orderly fashion.

Urinary frequency may be due to sensory or motor irritation or to complicating cystitis or prostatitis.

Dysuria may mean sensory irritation but usually indicates a coexisting infection.

Urgency of urination may result from sensory irritation (sudden, overwhelming desire to void, often with pain) or from motor irritation (unexpected micturition without much warning or discomfort).

Urinary incontinence may be merely an exaggerated urgency, as in multiple sclerosis, or it may take the form of genuine incontinence (continous dribbling with an empty, contracted bladder) or of a false (overflow, paradoxical) incontinence in which a full bladder intermittently expels a part of its contents without the patient's consent. True incontinence is rare and means complete motor and sensory destruction when mechanical causes (sclerosis, infiltration or destruction of both sphincters, fistula) can be excluded. Overflow is due to loss of sensation, so that the patient is happily unaware of his distended bladder.

Urinary retention may mean spasm of one or both sphincters (irritative motor lesion) or it may result from paralysis of the detrusor muscle, usually from loss of sensation rather than from true motor paralysis.

Most commonly urinary frequency, particularly as nocturia, and difficulties in controlling the stream (retention, urgency, incontinence) are first noted by the patient.

Clinical Findings.—It is most convenient here to divide the cases into the chronic, slowly progressive and the acute type. The former are usually due to degenerative diseases, such as tabes, subacute combined degeneration and neoplasm; the disturbance of sensation most often predominates. In the latter, because of the nature of the underlying disease, there is a combined motor and sensory lesion. Pure motor lesions are rare.

The sequence of events in cases of the former type is usually as follows: There is an initial loss of sensation which at first causes only infrequent micturition. As a result, the bladder becomes somewhat dilated, the pressure required to provoke the desire to void increases, and this increase in pressure ultimately interferes sufficiently with the venous circulation of the bladder to cause some atrophy of the wall. This is seen with the cystoscope as a fine, threadlike trabeculation. The internal sphincter, being but a part of the detrusor muscle, shares in this atrophy and appears to be relaxed or gaping. The loss of sensation reduces the discomfort of cystoscopy, often removing it entirely, and as a consequence the pressure which must be exerted by the cystoscopic irrigating medium to evoke a contraction of the detrusor muscle is much increased. As a result the medium trickles out of the end of the instrument instead of being ejected powerfully, as is normal (loss of expulsive force).

As the process goes forward both the reduction of sensation and the secondary atrophy of the wall of the bladder further reduce expulsive force so that residual urine and ultimately overflow (false) incontinence

develop. The mechanism of micturition in overflow incontinence probably depends on the fact that only very powerful contractions of the bladder reach consciousness through the impaired sensory mechanism. As a result the vesical ganglia take over the process, and a part of the contents of the bladder is expelled from time to time unconsciously by stimuli which do not reach consciousness.

The end-result of the process is, of course, dilatation of the ureters and kidney pelves, hydronephrotic atrophy and uremia. Rarely does a fatal issue ensue without the development, as usually happens in the presence of urinary stasis, of an infection which hastens the process.

In cases in which the dominant lesion is not sensory impairment the picture may be quite different. Occasionally one sees both sphincters relaxed and the wall of the bladder thickened and contracted (true incontinence, which is more often mechanical in origin); at other times one finds spasm of the sphincter with urinary retention or a contracted, irritable bladder with, nevertheless, some retention or difficulty in urination.

No comment on findings is complete without some mention of cystometry, the importance of which has been so much emphasized by Rose.[17] A cystometrogram is made by charting the pressure which results within the bladder from its intermittent distention with measured amounts of fluid, recording the pressure at which the patient feels the desire to void, at which severe pain occurs and at which fluid is expelled around the catheter. Oftentimes definite conclusions may be drawn by comparing the chart with the normal. In cases of sensory impairment the pressure rises more slowly than normal, the desire to void is evoked only by an unusually high pressure and pain may not be felt at all. On the other hand, with the hyperirritable bladder of certain phases of multiple sclerosis the desire to void may appear early and the pressure rise quite high.

While a combination of cystoscopy and cystometry will usually establish the fact that neurogenic vesical dysfunction exists, the exact determination of the type of disease present in the nervous system depends on a careful neurologic examination.

Nervous Diseases and Their Disturbances of the Bladder.—Diseases of the Brain: Owing to the confusion which obtains as to the existence of various centers for micturition and their function, it is natural that there should be considerable uncertainty as to the effects of lesions of the brain on urination. This uncertainty is fostered, as has already been pointed out, by the fact that the centers and tracts in the brain are bilaterally symmetrical so that a unilateral lesion produces transitory

17. Rose, D. K.: Cystometric Bladder Pressure Determinations, J. Urol. **17**: 487, 1927; Various Cystometrograms and Their Interpretation, ibid. **27**:207, 1932.

effects, if any (Czylharz and Marburg[18]). In most of the reported cases of vesical dysfunction due to disease of the brain one is left in doubt as to the possibility that local disease, notably prostatic hypertrophy, has caused the disturbance in the bladder, since most reports have been made by neurologists and have not been accompanied by cystoscopic observations.

Function of the bladder has been altered chiefly by hemorrhage, neoplasms, inflammation and trauma to the brain, and in the cases from which conclusions have been drawn the area of the brain involved has been so large as to cast doubt on the validity of those conclusions.

Elsberg[19] found that in 75 per cent of his cases of disturbed urination associated with cerebral disease the cause was to be found not in a lesion of a center but in psychic disorders and disturbances of consciousness (stupor, somnolence and coma). This leaves 25 per cent in which the dysfunction must be attributed to involvement of some center or pathway.

Other writers have attempted to attribute definite urinary disturbances to lesions of definite areas in the brain but such conclusions are more or less conjectural.

Lesions of the frontal cortex are said to cause, at first, retention and, later, automatic micturition (Minkowski,[20] Bechterew and his associates,[21] Hamburger,[22] Czylharz and Marburg,[8] Lichtenstern and Marburg[23]).

Disease of the thalamus produces sensory impairment (Lichtenstern and Marburg), and the resultant dysfunction is like that following disease of the spinal cord. It should be noted, too, that the disturbance with frontal lesions follows the same course as that of experimental division of all nerves of the bladder or of the spinal cord and points to a disturbance of sensation as a causative factor.

Langworthy and Kolb[24] observed an increase in the tonus of the detrusor muscle in decerebrate animals and compared it to the well

18. Czylharz, E., and Marburg, O.: Ueber cerebrale Blasenstörungen, Jahrb. f. Psychiat. u. Neurol. **20**:134, 1901.

19. Elsberg, C. A.: The Frequency and Character of Bladder Disturbances in New Growths of the Brain and Spinal Cord, Ann. Surg. **84**:509, 1926.

20. Minkowski, M.: Ueber cerebrale Blasenstörungen, Deutsche Ztschr. f. Nervenh. **33**:127, 1907.

21. Bechterew and Mislawsky: Die Hirncentra für die Bewegung der Harnblase, Neurol. Centralbl. **7**:505, 1888. Bechterew and von Meyer: Ueber die Rindencentra Sphincteris Ani et Vesicae, Neurol. Centralbl. **12**:81, 1933.

22. Hamburger: Ueber spinale und zerebrale Störungen der Harnblaseninnervation, Zentralbl. f. inn. Med. **25**:374, 1904.

23. Lichtenstern, R., and Marburg, O.: Ueber initiale Blasenstörungen bei organischen Nervenkrankheiten, Ztschr. f. urol. Chir. **38**:145, 1933.

24. Langworthy, O., and Kolb, L. C.: The Encephalic Control of Tone in the Musculature of the Urinary Bladder, Brain **56**:371, 1933.

known decerebrate rigidity of voluntary muscle. Bechterew and his co-workers [21] observed a similar disturbance clinically from a lesion of the optic thalamus, while Minkowski, Czylharz and Marburg and Lichtenstern and Marburg found the same disorder with a lesion of the corpus striatum (chorea). It results in what Minkowski [20] called "tonic" incontinence. Schwarz [25] described retention with dysuria in the same disease.

Lesions of the corpus pallidum (Parkinson's disease) are said at times to cause hypertonicity of the external sphincter with retention of urine (Lichtenstern and Marburg [23]).

McClintic [26] described "spastic paralysis with retention" in disease of the midbrain.

It is evident from this brief summary of a fairly extensive literature that there is still room for much study of vesical dysfunction due to diseases of the brain and that conclusions regarding them must be guarded. It is certain, however, that the majority of such disturbances are due to disturbances of the psyche, or consciousness, or of sensation and that disorders of the bladder are of no practical value as localizing signs. The treatment is, of course, that of the underlying disease.

Diseases of the Spinal Cord: Here knowledge is more accurate. Lesions of the spinal cord disturb micturition by irritating, injuring or destroying parts of the nervous mechanism of the bladder. The frequent and important lesions are largely sensory because of the presence of a motor mechanism situated in the wall of the bladder which is usually left intact.

One may take traumatic myelitis as a typical disturbance because so much is known about its effects, both from experimental studies and from many careful observations of those wounded in war. The following description is a composite picture drawn from the reports of Barrington [7] Head and Riddoch,[27] Holmes,[28] Minkowski,[20] Plaggemeyer,[29] Walker,[30] Adler [31] and others:

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25. Schwarz, O.: Die nervöse Versorgung der Harnblase, in von Lichtenberg, A.; Voelcker, F., and Wildbolz, H.: Handbuch der Urologie, Berlin, Julius Springer, 1926, vol. 1, p. 426.

26. McClintic, C. F.: The Clinical Neurophysiology of the Automatic Urinary Bladder and Enuresis, J. Urol. **20**:267, 1928.

27. Head, H., and Riddoch, G.: The Automatic Bladder, Excessive Sweating, and Some Other Reflex Conditions in Injuries of the Spinal Cord, Brain **40**:188, 1917.

28. Holmes, G.: Observations on the Paralyzed Bladder, Brain **56**:383, 1933.

29. Plaggemeyer, H. W.: Shell Fractures of the Spine, J. A. M. A. **73**:1599 (Nov. 22) 1919.

30. Walker, J. W. T.: The Bladder in Gunshot Injuries of the Spinal Cord, Lancet **1**:173, 1917.

31. Adler, A.: Ueber organisch (kortikale) und funktionellnervöse Blasenstörungen, Deutsche Ztschr. f. Nervenh. **65**:72, 1920.

On injury to the spinal cord above the lower sacral segments severe enough to produce a transverse lesion there ensues a period of flaccidity lasting from ten to twenty-one days resulting in retention and then a continuous dribbling overflow. Tone begins to return to the detrusor muscle and sphincters in from five to seven days, at which time the sphincters become somewhat hypertonic. Reflex excitability of the detrusor muscle is incomplete for from three to five weeks, when reflex incomplete involuntary urination develops if given an opportunity. If the lesion is below the midthoracic area the patient is aware of distention of the bladder (sensory fibers of the hypogastric). If it is above that level, he is not. Opinion is about equally divided as to whether a lesion of the sacral nuclei is distinguishable by its effects on the bladder from disease at a higher level, some maintaining that destruction of the sacral segments results at once in a flaccid bladder in which periodic urination never develops while others deny this and believe it will occur, if given an opportunity, regardless of the level of the lesion.

Elsberg [19] pointed out that in all lesions of the spinal cord of a transverse type (trauma, tumors of the cord) the frequency of disturbances in the bladder increases as the level of the lesion descends, being least frequent with lesions of the cervical and most frequent with those of the sacral portion of the cord. He and Stookey found that the severity of disturbance in the bladder is proportional to the degree of the somatic changes, especially of the sensory changes.

The cystoscopic findings are essentially those described for neurogenic dysfunction in general, with minor variations according to the stages and severity of the lesion. Particular emphasis has been laid on the absence of diverticula, ulcers and dilatation of the mouths of the ureters in uncomplicated cases (Plaggemeyer,[29] David,[32] Fullerton [33]).

The effects of traumatic myelitis on the bladder cannot be distinguished from those of any other suddenly appearing transverse lesion of the cord, nor is there any essential difference between the effects of trauma to the cord associated with fracture of the spine and those due to hemorrhage into or stretching of the cord without bony injury.

Tabes dorsalis is one of the commonest causes of neurogenic vesical dysfunction, being responsible for 75 per cent or more of the cases. Since the disease is predominantly sensory (degeneration of the posterior columns), it affords probably the closest approach to a pure sensory lesion which one may encounter. As might be expected, the first symptom is due to lack of perception of fulness in the bladder and takes the form of infrequent urination, which is usually not noted by

32. David, V. C.: The Management of the Urinary Tract of Paraplegic Patients, J. A. M. A. **76**:494 (Feb. 19) 1921.

33. Fullerton, A.: A Note on the State of the Ureters and Their Orifices in Cases of Gunshot Wounds of the Spine, Brit. M. J. **1**:124, 1919.

the patient. Incomplete emptying early ensues, also because of the sensory defect, and is aggravated by the effect of continuous partial distention on the muscle of the bladder (congestion, atrophy), which is an effect in which the internal sphincter shares (gaping, relaxation). The resultant decrease in expulsive force coupled with lack of desire may result in acute retention rather early in the disease if the prostate is slightly enlarged or contracted. More often overflow incontinence ensues. Rarely, spasm of the sphincter may occur (von Frankl-Hochwart [15]), although one always considers mechanical obstruction in such a case.

Hydronephrosis occurs relatively late compared with that which accompanies mechanical obstruction, because the pressure generated in the persistently full tabetic bladder is relatively low; but it does occur and, when complicated by infection, is a common cause of death. The cystoscopic findings are those described in the general survey—an insensitive, sluggish, relaxed bladder.

Multiple sclerosis also commonly disturbs the function of the bladder; while with tabes the bladder is sluggish, with multiple sclerosis it is usually overactive. Irritative changes predominate, probably owing to lesions of the pyramidal tract and are expressed as increased tone sometimes of the detrusor muscle (Oppenheim,[34] von Frankl-Hochwart and Zuckerkandl,[35] Collins and Baehr [36]) and sometimes of the sphincters. The sensory impairment which is usually present increases the effect of the motor irritation by lessening the patient's consciousness of it. All are familiar with the typical incontinence in this disease; the condition of retention and hyperesthesia (Braasch,[37] Smith,[1] von Frankl-Hochwart [15]) is less well known. The whole picture is complicated by the frequent presence of ataxia of the bladder (von Lichtenberg [38]). The cystoscopic findings are, of course, variable.

The subacute combined degeneration of pernicious anemia produces in many instances (13.6 per cent, according to Kretschmer [39]) a dis-

34. Oppenheim, G.: Ueber klinische und anatomische Frühstadien der multiplen Sklerose, Neurol. Centralbl. **29**:668, 1910.

35. von Frankl-Hochwart, L., and Zuckerkandl, O.: Die nervösen Erkrankungen der Harnblase, Vienna, A. Hölder, 1898.

36. Collins, J., and Baehr, E.: Disseminated Sclerosis, Am. J. M. Sc. **148**:495, 1914.

37. Braasch, W. F.: Data with Regard to Lesions of the Nerves of the Urinary Tract, J. Urol. **13**:383, 1925. Braasch, W. F., and Thompson, G. J.: Treatment of the Atonic Bladder, Tr. Am. A. Genito-Urin. Surgeons **27**:99, 1934.

38. von Lichtenberg, A.: Personal communication to the author.

39. Kretschmer, H. L.: Spinal Cord Bladder Occurring in Pernicious Anemia, J. Urol. **6**:195, 1921.

turbance of the bladder much like that of tabes and usually eventuates in overflow incontinence. The marked similarity in the effects of these two diseases on the function of the bladder fortifies my belief that by far the most important nerve lesions are those which impair sensation, since tabes, a sensory disorder, in its effect on the bladder resembles closely subacute combined sclerosis, which is both sensory (posterior columns) and motor (pyramidal tracts).

Amyotrophic lateral sclerosis also occasionally disturbs micturition (Lendrum and Moersch [40]), but I have no knowledge of the nature of the disturbance.

Progressive muscular dystrophy caused "complete incontinence" in a case of McKendree's,[41] probably because the external sphincter shared in the generalized weakness of the voluntary muscles.

The disorders of the bladder in cases of syringomyelia are like the underlying lesion, rather irregular. They occur frequently in the disease (Jelliffe and White [42]) and may early take the form of sensory irritation (Gilbert Smith [43]), spasm of the sphincters and retention (von Frankl-Hochwart [15]) or paralysis of the sphincter with incontinence, probably overflow incontinence due to anesthesia, as in tabes.

Neurogenic vesical dysfunction is fairly common in cases of poliomyelitis, although it has been the subject of little comment. Toomey [44] found it in 15 per cent of 386 cases which he studied. He found the bladder flaccid and unresponsive to local stimuli. Bugbee,[45] however, reported a case of painful retention requiring cystostomy. Toomey observed that there was often no somatic disturbance in the segments corresponding to the bladder and attributed its involvement to a toxic effect on the sympathetic apparatus. Dr. J. C. McKinley [46] has informed me that, in his experience, disorders of the bladder are commoner with severe grades of paralysis of the lower extremities and are usually painful, indicating that the causative lesion is in the motor apparatus only (cells of the anterior horns). The infrequency with which disturbances of the

40. Lendrum, F. C., and Moersch, F. B.: Neurologic Diagnoses in Two Hundred and Fifty Cases of Cord Bladder, J. A. M. A. **102**:658 (March 3) 1934.

41. McKendree, C. A.: Combined Dystrophy with Loss of Vesical Control, Neurol. Bull. **1**:61, 1918.

42. Jelliffe, S. E., and White, W. A.: Diseases of Nervous System, Philadelphia, Lea & Febiger, 1915, p. 355.

43. Smith, G. G.: Bladder Disturbances Due to Nerve Lesions, J. A. M. A. **69**:1323 (Oct. 20) 1917.

44. Toomey, J. A.: The Intestine and Urinary Bladder in Poliomyelitis, Am. J. Dis. Child. **45**:1211 (June) 1933.

45. Bugbee, H. G.: Paralysis of the Bladder in Poliomyelitis, J. Urol. **13**:333, 1925.

46. McKinley, J. C.: Personal communication to the author.

bladder are mentioned is probably due to the fact that they are transitory, usually disappearing in three or four days, even without treatment (Toomey).

Arteriosclerosis within the spinal cord may also interfere with normal micturition (Lendrum and Moersch [40]) in a fashion reminiscent of tabes dorsalis, although its effects are usually less pronounced and can be identified by the age of the patient and the patchy character of the somatic disturbances.

Congenital defects of the spinal cord are of especial interest in a consideration of neurogenic disorders of the bladder and are usually associated with spina bifida, either occult or manifest. Two chief clinical types may occur in either form. In the first, the rectum is often involved; there are somatic disturbances, usually in the feet, and other congenital deformities are frequently present. This type is more common in frank spina bifida. In the second, the bladder alone is involved, the somatic segments being normally innervated. The relation between spina bifida and function of the bladder was pointed out by Fuchs.[47] In the first form there is an anomaly in or about the spinal cord, as in hydromyelia (Fuchs,[47] Oppenheim [34]), duplication of the cord or a cleft in its dorsal surface below the defect in the spine (Scharnke,[48] Wodak [49]) or an abnormal pad of fat compressing the cord. In addition, Penfield and Cone [50] suggested that the presence of a defect in the spine prevents normal ascent of the sacral posterior roots, injurying them by traction and producing the disturbance of the nerves.

In the second group, the absence of somatic disturbances makes it necessary to assume an associated congenital defect in the peripheral nerves to the bladder, or, according to Mertz,[51] in the parasympathetic system, rather than an anomaly of the cord per se. The second group will be discussed with lesions of the peripheral nerves.

While spasm of the sphincters may occasionally result from the myelodysplasia of spina bifida, the usual result is hypesthesia or anesthesia of the bladder with partial retention and later with overflow incontinence. True incontinence is rather rare.

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47. Fuchs, A.: Ueber Beziehungen der Enuresis nocturna zur Rudimentärformen der Spina bifida occulta (Myelodysplasia), Wien. med. Wchnschr. **60**:1569, 1910.

48. Scharnke: Enuresis und Spina bifida occulta, Arch. f. Psychiat. **53**:43, 1914.

49. Wodak, E.: Ueber Enuresis mit Myelodysplasie und Bemerkungen zur Enuresis überhaupt, Jahrb. f. Kinderh. **87**:47, 1918.

50. Penfield, W., and Cone, W.: Spina Bifida and Cranium Bifidum, J. A. M. A. **98**:454 (Feb. 6) 1932.

51. Mertz, H. O.: The Relation of Spina Bifida Occulta to Neuromuscular Dysfunction of the Urinary Tract, J. Urol. **29**:521, 1933.

THE PERIPHERAL NERVES

In considering the effects of lesions of the peripheral nerves on the function of the bladder one is confronted by the same difficulties presented by lesions of the spinal cord or brain, i. e., each nerve is mixed in its function so that most lesions produce combined motor and sensory disturbances. Moreover, one cannot determine precisely from the type of disturbance of the bladder whether the lesion is in the nerve roots, their trunks or in the ganglia.

Since all three of the nerves contain sensory fibers, an irritative lesion of any one would produce an irritable, uncomfortable bladder. The presence and type of disturbance from irritation of the motor component of one of the nerves would be difficult to predict. In the case of the hypogastric nerve no definite effect would be expected; irritation of the pelvic motor fibers would probably enhance the power and frequency of the contractions of the bladder. Irritation of pudic nerves would probably cause spasm of the external sphincter and retention. Irritation of the sacral roots (caudal neuritis: Lendrum and Moersch [40]) would disturb both the pudic and the pelvic elements, producing frequent, painful, difficult micturition or painful retention.

Such lesions are rarely described, probably because their symptoms resemble those of infection and because the irritative phase is likely to be transitory, terminating shortly in recovery or in a destructive lesion. Again drawing on experiments done on animals, one would expect only a transitory frequency from destruction of the hypogastric nerve. Destruction of the pudic nerve may cause a transitory, incomplete leakage of urine, while damage to the pelvic nerve is alone likely to be serious, resulting in anesthesia with overflow incontinence.

In general, four types of derangements of the nerves of the bladder are encountered: mechanical, inflammatory and congenital anomalies and those due to uncertain causes.

The mechanical type is exemplified by injury to the pelvic nerve from pressure by the presenting part during labor or by the retroflexed pregnant uterus (Barrington [7]). The same nerve may be injured directly during surgical intervention, particularly for carcinoma of the rectum or by the Wertheim operation for uterine cancer. In the same group should be included stretching of the sacral roots by forced flexion of the spine in the sitting position (Spiller [52]) and of traction or compression of these same roots in certain cases of spondylolisthesis (Helwig and Burns [53]). The usual result is retention (painless) and, later, overflow.

52. Spiller, W. G.: Congenital and Acquired Enuresis from Spinal Lesions, Am. J. M. Sc. **151**:469, 1916.

53. Helwig, F., and Burns, J. E.: Bladder Disturbances in Relation to Abnormalities of the Lumbosacral Spine, Tr. Am. A. Genito-Urin. Surgeons **24**:323, 1931.

Rose [10] expressed the belief that many of the puerperal disturbances of the bladder are due to compression of the pudic nerves during labor, but the slight and transitory effects of their section both experimentally and clinically make this doubtful.

Extension from malignant lesions in the vicinity, especially those of the uterine cervix, the rectum, the bladder and the prostate, may also invade the nerves of the bladder. Their effects are usually irritative.

Inflammatory processes may involve the peripheral vesical innervation. This may occur as an extension of a local inflammation, as after posterior excision of the rectum, either shortly after the operation (acute inflammation) or remotely (constriction of scar tissue); it may be a part of a generalized diabetic neuritis or alcoholic neuritis, or it may be a toxic manifestation complicating an infectious disease, such as poliomyelitis (Toomey [44]), scarlet fever, measles, diphtheria or pneumonia (Campbell [54]).

Mention has already been made of the disturbances of function of the bladder which may accompany the anomalies of the spinal cord often associated with spina bifida and which are associated with abnormalities of the somatic innervation. Similar disturbances are also seen in spina bifida occulta, often without evidence of any dysinnervation except in the bladder. Here one is forced to assume that there is a defect in the peripheral innervation of the bladder, probably in the vesical plexus itself, since the rectum may function normally and somatic changes may be absent.

The usual clinical picture produced by all of these lesions of the peripheral nerves is that of a variable degree of sensory loss with overflow incontinence. True incontinence, retention and irritative phenomena are less frequent. The cystoscopic findings correspond to those of disease of the spinal cord.

In the group of uncertain etiology must be placed the incontinence observed in hyperthyroidism by Stern [55] and by McClintic, which the latter explained as the result of relaxation of the sphincters by epinephrine in the absence of the thyroxine which normally antagonizes it. Pearson [56] reported altered function of the bladder in tuberculous meningitis, but I suspect that this should be attributed to disturbance of the sensorium.

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54. Campbell, M. F.: Neurogenic Vesical Dysfunction in Children, J. A. M. A. **93**:183 (July 20) 1929.

55. Stern, H.: Ein bisher nicht beschriebenes Zeichen von Hypothyreosis, Berl. klin. Wchnschr. **51**:318, 1914.

56. Pearson, S. V.: Tuberculous Meningitis in Adults Occurring as a Terminal Event in Chronic Pulmonary Tuberculosis, Clin. J. **21**:154, 1902.

DIAGNOSIS

The differential diagnosis between neurogenic vesical dysfunction and organic disease of the lower portion of the urinary tract is of considerable importance, not alone because of the wide variety of symptoms which the former may cause but also because the latter lesions so often coexist with the former, either independently or as a result of them.

Whenever there is reason to suspect the existence of neurogenic vesical dysfunction the first step should be a painstaking neurologic examination since in the vast majority of cases definite evidence of disease elsewhere will be found. This often fails to apply with spina bifida occulta, in which a roentgen examination of the lumbosacral portion of the spine is of great assistance, and to the diseases of the peripheral nerves and ganglia, in which the history often determines the diagnosis.

Two types of local disease of the bladder most often give rise to confusion, namely, obstruction of the neck of the bladder and infection. The former comes into consideration in cases of urinary retention and is best settled by cysto-urethroscopy. Coexistence of obstruction of the vesical neck and neurogenic dysfunction is not infrequent. It should be remembered that if disease of the nerves has impaired the function of the bladder by impairing expulsive force the effect of obstruction of the neck of the bladder is intensified so that a median bar, for example, which would ordinarily cause no symptoms, may produce complete urinary retention. In such a case the condition may respond to the usual treatment for the bar. The diagnosis is made with the cystoscope and is based on finding prostatic hypertrophy or fibrosis together with one or more of the changes of neurogenic dysfunction, usually reduction of sensation and expulsive force.

Infection as a diagnostic problem usually occurs in irritative lesions; the mere presence of pus in the urine does not settle the question since infection is frequently a complication of neurogenic dysfunction if retention is present. Cystoscopy usually determines the diagnosis if neurologic and urinary findings are given due consideration.

In the presence of true incontinence it is important to distinguish between a lesion of a nerve and an infiltration of both sphincters by carcinoma or scar tissue in such a fashion as to hold them open and cause leakage. Occasionally a stone impacted in the prostatic urethra has a similar effect. In women vesicovaginal and ureterovaginal fistulas and ectopic ureters opening outside the bladder must be considered.

With overflow incontinence, the history and rectal, neurologic and cystoscopic examinations, serve to distinguish the neurogenic from the mechanical variety.

The most serious difficulty in differential diagnosis arises in the presence of so-called primary atony of the bladder, in which one finds

urinary retention without evidence of obstruction, spasm of the sphincter or sensory disturbances (Braasch,[57] Fronstein,[57] Geraghty [58]). This condition has been attributed to senile atrophy of the detrusor muscle, to a toxic degeneration of the muscle of the bladder, to fatty infiltration of the detrusor muscle and to replacement of the fibrous tissue of the muscle fibers resulting from arteriosclerosis or inflammation. Gundrum [59] has described a familial type. It is diagnosed by exclusion.

The use of the cystometer has been widely heralded as a valuable aid in the differentiation of neurogenic dysfunction from local lesions, some observers even claiming to be able to identify exactly disease of the nervous system from the reading of the pressure of the bladder. It is a poor substitute for a careful neurologic and cystoscopic examination; moreover, it will often fail to differentiate between the disturbances of tabes dorsalis, subacute combined sclerosis, myelitis and disease of the pelvic nerve or vesical plexus, nor will it distinguish the irritable bladder of acute cystitis from that, say, of early multiple sclerosis. However, it remains an interesting matter for further study.

TREATMENT

Treatment must be directed along two lines, that is, at the underlying disease and at the local condition of the bladder. No attempt will be made to discuss the former, except to emphasize the fact that cure of the underlying disease of the nervous system will often cure the disorder of the bladder, as in the case of tumor of the spinal cord or brain, while benefit from the treatment, particularly in tabes or subacute combined degeneration may or may not help the condition in the bladder.

The importance of the local treatment needs no more emphasis than to point out that many patients with neurogenic vesical dysfunction die of renal failure and infection long before the underlying disease becomes a serious menace or even after it has begun to improve.

Irritative Lesions.—In cases characterized by urinary frequency and urgency without retention local treatment is of lesser importance. It should be based on a study of any complications not related to the nervous disease, such as prostatitis or unrelated pyelitis or cystitis, since these may be entirely responsible for the symptoms. I recall in this connection the case of a young man with multiple sclerosis, marked urinary frequency and dysuria, whose urinary symptoms disappeared after prostatic massage. Beyond such therapy relatively little can be

57. Fronstein, R.: Die primäre Harnblasenatonie, Ztschr. f. Urol. **23**:445, 1929.

58. Geraghty, J. T., in discussion on Smith, C. G.: Bladder Disturbances Due to Nerve Lesions, J. A. M. A. **69**:1336 (Oct. 20) 1917.

59. Gundrum, F. F.: Familial Bladder Atony, J. A. M. A. **78**:411 (Feb. 11) 1922.

done except for the nervous disease. Antispasmodics, such as tincture of hyoscyamus, benzl benzoate and papaverine, may be of some value.

Urinary Retention.—When urinary retention without incontinence is present, obstruction of the neck of the bladder should be excluded from the diagnosis, it being borne in mind that a small fibrous median bar or hypertrophy may produce retention which may be relieved by dilatation or transurethral resection.

If retention is found one should remember its importance as a predisposition to infection and take every precaution to combat it with urinary antiseptics, the ketogenic diet and lavage of the bladder. Asepsis must be strictly observed.

In many, if not most, cases of retention the cause is found in a reduction of sensation which causes at first a distention of the bladder through the lack of knowledge that it is full; later the distention causes atrophy of the detrusor muscle and retention through lack of expulsive force. When patients are seen when the condition is in the early stage it is sometimes possible to secure emptying of the bladder merely by directing the patient's attention to it and training him to void at regular hours during the day and night, using an alarm clock to awaken him if necessary.

If atrophy of the detrusor muscle is under way but not advanced, drugs may perhaps be of value, either stimulators of the parasympathetic nerves, such as physostigmine or pilocarpine, or those that paralyze the sympathetic system, such as acetyl choline or, preferably, its more stable derivative, acetyl beta methyl choline chloride. The by-effects of these drugs are, unfortunately, often so unpleasant or even dangerous as to prevent their continuous use, but they are most useful in starting emptying of the bladder when damage is not too serious.

In cases in the more advanced stages a combination of the aforementioned methods with intermittent catheterization two or three times daily may rest and stimulate the bladder sufficiently to permit resumption of emptying. A period of treatment with an indwelling catheter might be helpful.

When all the methods fail and obstruction of the neck of the bladder is absent, surgical methods should be considered if the patient is intelligent and some sensation remains in the bladder. Learmonth and Braasch [60] recently reported excellent results in such cases from excision of a part of the hypogastric plexus (presacral neurectomy) predicated on the assumption that since impulses traveling along these nerves inhibit detrusor contraction their division will enhance the power of the detrusor muscle. I have thought that a patient who can be relieved by this method

60. Learmonth, J. R., and Braasch, W. F.: Resection of the Presacral Nerve in the Treatment of Cord Bladder, Surg., Gynec. & Obst. **51**:494, 1930.

could probably be relieved by the regimen prevously outlined, and I have employed surgical intervention only when the latter has failed. I have then supplemented it by cystostomy in order to give the bladder a period of physiologic rest in which to recover its tone. In case of the 3 patients thus far treated the results have been excellent. The patients have been trained to urinate "by the clock" in an effort to insure permanence of the relief.

Incontinence of Urine.—When overflow incontinence is present the problem is similar to that already discussed, with the additional factor that the detrusor muscle is usually so badly damaged that anything short of presacral neurectomy with cystostomy is likely to be futile.

True incontinence is happily rare. If it is accompanied by complete anesthesia of the bladder the patient is doomed to the use of a penis clamp or incontinence bag unless circumstances warrant implantation of the ureters into the sigmoid colon, a procedure which must surely be considered, but only if rectal sensation and function are normal.

If true incontinence is accompanied by good sensation in the bladder (which may be tested by distention of the bladder through a catheter or, better, by cystoscopy without anesthesia), one of the various plastic operations on the sphincter may be tried (suture of the levators behind the sphincter for men, as advocated by Keyes, the Gersuny or Thomsen operations for women or the Stoeckel procedure or one of its modifications or a gracilis transplantation for patients of either sex).

Traumatic Myelitis.—The methods thus far outlined are obviously limited to the treatment of incomplete lesions in which some sensation in the bladder remains. For the treatment of complete lesions which so often accompany traumatic or infectious myelitis separate comment is required. Here there is no control whatever over the bladder, and for a time at least the condition of the patient prevents any but very conservative measures. The usual sequence of events is a flaccid, paralyzed bladder from which a continuous overflow begins in from twenty-four to seventy-two hours. Many investigators now believe that catheterization should be avoided at all costs in such cases, and emptying of the bladder encouraged by intermittent suprapubic pressure and by stimulation of the external genitalia. Infection can thereby often be avoided and the development of an automatic function of the bladder in from three to five weeks anticipated. When this method is used great care is required to prevent continual wetting of the patient, for fear of bed sores. Cumming [61] found caudal anesthesia of value in initiating emptying of the bladder in cases in which manual expression could not be

61. Cumming, R. E.: Structural and Functional Changes in the Urinary Tract Following Focal Cord Lesions, J. A. M. A. **99**:1998 (Dec. 10) 1932.

accomplished because of spasm of the sphincters. Mechanical or electric stimulation of the external genitalia is often helpful in initiating micturition.

Unfortunately most of the patients seen in the University Hospital have already been catheterized and have become infected, so that other methods must be used, since to allow the overflow of an infected bladder is to invite serious pyelonephritis. I believe that in such a situation, if there is any possibility of functional recovery, intermittent or continuous catheterization should be done until the condition of the injury permits a cystostomy, as suggested by Priestley.[62] Later, if the patient recovers sufficiently to walk, function of the bladder may improve correspondingly and permit closure of the cystostomy opening. If partial retention then occurs, presacral neurectomy may be considered. If sensation does not return, the tube may be left in place, keeping the patient dry and reducing the danger of infection.

If the condition of the patient is such as to make death certain, catheterization is the method of choice.

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62. Priestley, J. T.: The Spinal Cord Bladder, J. Urol. **21**:635, 1929.

PSYCHOLOGY AND THE UNIVERSITY

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There is reason to believe that in coming years the university which contributes most to the advancement of learning and the cultivation of the human spirit will be the one which develops and sustains the greatest school of psychology. And with psychology there will necessarily be furthered an underlying physiology and an overlying sociology.

Psychology's immediate destiny is promising because the necessary conditions for a significant acceleration of its growth are for the first time present. These conditions need not be specified exactly here. Suffice it to say that they consist of certain recently discovered facts, certain recently devised methods, certain recently constructed theories and, most important of all, certain recently advanced basic propositions which are sufficiently comprehensive and dynamic to serve as a conceptual foundation for the development of this science.

The advance of psychology is especially important because its interrelationships are so manifold that any discovery which it makes will immediately animate research and speculation in many other disciplines. To recognize this one has only to consider the mutual dependence of the sciences and the number of those that immediately wait on psychology—sociology, anthropology, criminology, pedagogy—or that are more remotely related—history, government, law. It is generally agreed that all social institutions are determined to a large extent by the interaction of human needs, sentiments and beliefs. Since these constitute the proper subject-matter of psychology, an economist is merely stating what seems too obvious for words when he says that a large proportion of economic and sociologic problems cannot be solved without psychologic data and that psychology is as necessary to social science as chemistry is to physiology.

Listen for a moment to the words of the social philosophers and judge whether they are not basing their proposals on certain suppositions—usually their private supposition—as to the nature of man. Is it not the function of psychology to correct or to verify such suppositions? Reflect on the increasing urgency of the problems of the neuroses and the psychoses. Consider the increasing number of physicians who are becoming convinced that many physical disturbances—perhaps even a majority of the less serious ones—are engendered by psychic states—mental shocks and conflicts, anxieties and depressions. Note how eagerly

the younger physicians are seeking information about psychologic mechanisms and the methods for their control. Consider the parents and the teachers in progressive schools who are turning hopefully to psychology for guidance. Think of the instructors in theological schools who advise psychology as an aid to pastorship. Take account of the historians and biographers who have come to realize that to achieve their ends they must acquire a deeper understanding of human motives. And do not neglect the artists and writers—the sensitive ones—who have always been the first to voice their intimations of emerging ideologies. Consider how many of them have "become psychologic," not only by adopting an analytic attitude toward the experiences which they shape but even by yielding their imaginations to modern theories. Consider the philosopher who has begun to suspect that the outcome of his finely articulated logic was partly predetermined by a certain concealed preference, a preference which was originally generated by a purely fortuitous set of circumstances—a childhood experience, let me say. Heed the zest of students, the many young men and women whose minds have been incited by the beckon of psychology. Consider especially the spiritual dilemmas of modern man, and note the widespread, unconscious tropism for psychology, not so much as a new sensation or as a terrain for scientific exploration but as a possible path out of conflict and into the right way. Consider how the psychotherapeutist is being conjured up as a wise merman or savior by the anxious, scarcely conscious longings of a bitterly shaken world; how willy-nilly he is being entrusted with a priestly function. Brood on all these things. Then ask yourself whether it is possible to maintain that today psychology does not occupy a vantage-point in the scheme of things.

If psychology is defined as the science which describes people and explains why they perceive, feel, think and act as they do, it must be admitted that a serious interest in the subject-matter of psychology is a distinctive characteristic of this generation but that, properly speaking, no science of the kind exists. That is, there is no comprehensive, unified body of essential facts, nor is there a satisfactory system of explanatory concepts. And because of this lack, philosophers, sociologists, historians, biographers and poets who deal with such matters must still to a large extent concoct their own psychologies.

But even if it is true that psychologists have not yet formulated a conceptual scheme which is acceptable to themselves or to others, they must have proposed some thought-provoking theories, for without stimulation of this kind the swelling current of imaginative concern with psychology would never have reached its present magnitude. And so one inquires: Who has contributed the germinal ideas? To find the answer to this question, one naturally turns to the universities, for it

has become their business to discover new facts and to evolve theories to account for them, as well as to impart knowledge.

In the big lecture-room Professor Piper is reading from his recent textbook a paragraph on the textual differences of images, while Wilson, quietly sucking a "life-saver" in the front row, wonders whether the cashier at the cafeteria was serious when she said he was ungentlemanly. In the basement of the laboratory Hoyer is setting up his camera to photograph the chromatophoral changes in the stellate cells of the leech's skin. He is thinking that he will have to miss Dr. Sill's talk at the seminar on the bodily turn of the white rat in a straight alley. Young Professor Faber, mincing along College Street, has just felt the approach of a revelation. There came suddenly to him the seminal idea that he might organize a frontal attack in the form of a comprehensive project for research to test the differences between blondes and brunettes. What faculty should he test first? This problem certainly has more pep in it than that of the increase of brightness in a circumscribed field. Miss Ischt and Miss Adnock, who share a room in the Social Science wing, are just tying up the four hundred questionnaires they have been tabulating, constituting a comprehensive study of the sentiments on such questions as whether co-eds should be allowed to smoke in the common room. The correlation, expressed by the Pearson ratio, between a liberal attitude in such matters and a "pleasing" personality as judged by four fellow classmates was 0.791473 ± 0.021591—an excellent result which confirms Professor Ohl's original assumption and assures Miss Adnock of her Ph.D. Miss Jelkoe is administering a test to the fourth grade at the Sulkin Progressive School. Her problem is the determination of the effect of a rest period on the performance in the Mulligan multimental intelligence test and the Vandifeldt O-Q emotional maturity test. Mannheim and roommate, Blitzen, are in the library foraging about in the psychology shelves. Mannheim has wagered that in the coming examination there will be a question on the apparent size of visual objects, whereas Blitzen is certain of a question on the theory of happiness as bright pressure in the epigastrium. From all this web of activity consideration of man as a human being has somehow escaped.

The truth which the informed are hesitant to reveal and the uninformed are amazed to discover is that academic psychology has contributed practically nothing to the knowledge of human nature. It has not only failed to bring light to the great, hauntingly recurrent problems, but it has no intention, one is shocked to realize, of attempting to investigate them. Indeed—and this is the cream of a wry jest—an unconcerned detachment from the natural history of ordinary mortals has become a source of pride to many psychologists.

It was about sixty years ago that psychology, by adopting the empirical, experimental attitude of physics and by developing its own methodology, established itself as a distinct science. Since it was necessary to begin by studying isolated fragments of experience and since the processes of sensation and perception were the fragments which were most susceptible to measurement, the pioneers commenced there. This original bias, firmly established by the classic experiments of such able men as Fechner, Helmholtz and Wundt, gave rise to the basic conception of a living being as a consciously receptive mechanism rather than an unconsciously motivated dynamism. This point of view persisted, and even today many of the best psychologic laboratories in this country remain bound to the ideology of introspectionism, the data of which are the reports which subjects make when presented with different physical stimuli—stimuli variously combined in space and time. As the field has become more confined, the methods more intricate and the theories more finely spun its devotees have lost contact with the great marches of thought, the biologic as well as the humanistic. To many outsiders these academic workers resemble vestal virgins—vestal virgins of unusable truth prolonging without profit the culmination of a spent impulse. They have, naturally, been accused of a half wilful triviality—recently, for instance, by Kohler in these words:

> Unfortunately, the adherents of introspection do not seem to trust their own procedure. At least, they must have agreed upon facing important problems as seldom as possible, since they are occupied mainly with describing the more remote and less exciting corners of experience, as, e. g., minor nuances of sensations, or the "glassy" appearance of certain parts of space and so forth. If all I have to do to develop the science of direct experience is to describe it, why then not attack the central facts of "mental life" at once, instead of scratching a little at the surface, or periphery, of it? There was a time in Germany, not very long ago, when people began to joke about psychology's ponderous discussion of trifles. And, indeed, it was strange to see how the description of a direct experience, what happens, for instance, during a single comparison of two tones or colors, could fill hundreds of pages without giving us the slightest positive idea about how the occurrence and accuracy of such a comparison might be explained. Even in a state of perplexity, a science can be highly interesting. But psychology, so far as it deals with direct experience by the method of introspection, has not only been a complete failure; it has also become boresome for all those who are not professionally connected with it.

A number of years ago behaviorism contracted its now notorious larynx as a polar reaction to introspectionism. It presented a fresh horizon, but one which proved no broader than that offered by the old field. Its metaphysical denial of consciousness, its provincial insistence on a radical positivism and its adherence to a stereotyped mechanistic formula have resulted in a self-limiting puritanical program of procedure which logically excludes all but the simplest problems—problems

such as the reflexive responses of bantam roosters. Luckily, men are escaping from behaviorism to better things.

More recently, there has arisen a heterogeneous group of workers bent on attacking personality—and a real attack it has proved to be. Armed with questionnaires, rating scales, pop-guns, mazes, peg-boards and numberless other mechanical contraptions, the testers have borne down on their subjects—so heavily, in fact, that the souls of their subjects have been forced to shelter. Hence, when one comes to examine the final results, arrived at by the most approved statistical methods, one discovers nothing of importance. The salt, it must be acknowledged, never landed on the bird's tail. Though it is encouraging to find that at last a considerable number of psychologists are occupying themselves with problems of personality, one is somewhat disquieted by the once-born, unripe confidence, the peculiar callousness of these testers—men who talk as though they had never been sensitized by a moving grief or joy. One wonders why they choose psychology as a field in which to labor.

This condensed review of academic psychology is purposefully critical. And it would be ungenerous if no mention were made of the natural limitations of man and the difficulties of the problem. One should realize that the blood of humanity is not thick enough to sustain more than a few men in greatness; that an odor of the mold almost always pervades academic enterprises; that psychology is in its infancy, and, furthermore, that there are many psychologists—introspectionists, behaviorists and personologists—who stand well outside the limitations which confine their fellow schoolmen. One should also recognize the signs of new growth that are about one—the great illumination, for instance, that gestalt psychology has shed. But even when all these things and more have been adduced, it must still be admitted that the great central problems have been neglected lamentably by the academic workers. The result is that the average psychologist knows no more than the layman about the behavior and inner life of his fellowmen. Indeed, the informed believe that he knows less. A concentration on sensory phenomena—the simpler peripheral reflexes of animals or the statistical manipulation of data obtained from questionnaires has led him away from his proper subject-matter—the driving forces which are basic to human nature. Hence, as Jung put it, a man who has wandered with a human heart through the world may be pardoned if his respect for the "corner-stones" of academic psychology is no longer excessive.

One is forced to acknowledge that university men have not contributed the ideas which have thrilled the imagination, nor have they provided the kind of answers that satisfy one's curiosity or meet one's needs. No. These have come from the medical psychologists—Janet,

Prince, Freud, Jung, Rank, Adler. One is tempted, indeed, to affirm that the technic of research, many of the revealed facts and a few of the theories advanced by the psychoanalysts represent the weightiest contribution ever made within a short space of time to an understanding of human nature. These workers have brought together more data pertaining to the lives of individual persons than has ever before been assembled, chiefly because they have been patient enough to listen every day over periods of months or of years to persons talking about themselves. They have discovered that many previously neglected phenomena—dreams, fantasies, the play of children, casual gestures, slips of the tongue and so forth—offer significant clues to the understanding of personality. And as an explanation of these and other once mysterious occurrences, they have proposed a comprehensive theory of unconscious psychic processes. Although the enlightened William James called this discovery "the most important step forward in psychology" because "it revealed to us an entirely unsuspected peculiarity in the constitution of human nature," most academic men still refute the notion on pragmatic or verbal grounds. With the help of this theory, however, psychoanalysts have gone far in the elaboration of a thoroughly dynamic scheme for the representation of personality, based on a concept of the interaction of forces, the simplification of which is the notion of instinctual drives inhibited or modified by other forces acting at the dominant center of the personality (the ego). They have demonstrated the subtly permeating influence of the sex instinct and of the will to power. They have proposed concepts to describe the changes that occur in the chosen objects and in the motor expressions of instinct—substitution, overcompensation, sublimation, regression. They have demonstrated the life-determining potency of inflexible infantile attachments and modes of response. They have shown how sentiments and unconscious complexes are generated. They have indicated how these sentiments may affect perception and judgment, how by rationalization they are commonly transformed into general principles. They have described typical family configurations, common clusters of traits of character and the emergent effects of the creative will. All this and much more has been accomplished—and accomplished during the span of the working life of a single man.

Since psychoanalytic formulations are especially designed to describe mental processes of which the ordinary citizen is seldom conscious, it is extremely difficult for him to reach any conclusion regarding their validity. To test the theories he must come in contact with persons who clearly manifest unconscious processes—with neurotic and psychotic patients—and he must train himself to focus on the revealing acts and words. I know no thorough student of psychoanalysis who, after observ-

ing the facts, has not been convinced that, in the main, the analysts are correct.

The emotional objections to psychoanalysis are understandable and predictable. They are chiefly due to the fact that analysts expose and dwell on just these primitive, aberrant and asocial inclinations which, since the dawn of culture, the higher will of man has attempted to destroy or, if not to destroy, to conceal from himself and others.

The intellectual opposition to psychoanalysis, however, though usually propelled by moral sentiments, brings formidable weapons to bear on the matter. In a nutshell it may be said that no critically minded person practiced in scientific research or in disciplined speculation can accept psychoanalysis on the basis of the writings of Freud or of any of his followers. The presentation of facts is inadequate; the speculation is irresponsible; verifications are lacking; conclusions are hastily arrived at, and concepts are hypostatized. It is only when one begins to practice psychoanalysis and confirming evidence accumulates that one comes to realize that Freud is a strange genius who has made some of the shrewdest guesses that have ever been recorded. It becomes apparent, furthermore, that analysts have not competently represented their own material. They have not been their own best advocates.

Psychoanalytic theories are attempts to explain the most complex aggregation of activities in nature—the mind of man. And they have been constructed by men who are for the most part untrained in the fundamental sciences. Is it a wonder that these theories resemble myths or metaphysical doctrines rather than authentic scientific formulations? One is not surprised to discover this or to find that the theories proposed by the leading analysts have, to a considerable extent, an autobiographic basis; that Freud in particular, like many another genius who has revealed hidden aspects of human nature, has viewed man with a markedly biased vision. This situation is to be taken for granted in a new science.

One is somewhat put off, to be sure, by the "smart Aleck" attitude of the freudian analysts, their simple-minded technical patter, their polymorphous perversities of logic, the magnanimous manner in which at certain times they set aside their critical faculties, their too-ready certitude, their hostility to research, their touchiness, their inability to get on with themselves or with others—in short, their pervading neuroticism. Such behavior is naturally repellant. It is an old truism, however, that one should not condemn a theory because its exponents are a bit "cracked."

The freudian psychoanalysts in Vienna, Berlin, London, New York, Chicago and Boston have formed societies which undertake to instruct students and to present those who finish a course of about three years'

training with certificates of competency to practice psychotherapy. But, since in America the rule is being generally adopted that to be eligible for such training one must have completed four years of medicine and two years of hospital work, there is a long row to hoe before one can be educated in this branch of knowledge.

At present, as part of the general drift toward psychology, an increasing number of expectant young men, thrilled by the strong invitation offered by the problem, are seeking a comprehensive knowledge of psychology. What has the university to offer? As it stands today, a young man or a young woman who wishes to learn psychology, for its own sake or because of its application to other fields, must pursue one of two courses: become a graduate student in psychology at a university or enter a medical school and after some further experience apply for psychoanalytic training.

If the student chooses to work for the degree of Doctor of Philosophy in psychology, he soon discovers that the subject-matter is divided into separate fields, each with its own terminology based on different fundamental assumptions. What he learns in one classroom cannot be related to what he learns in another, because each instructor mulls his own dream-world between his ears. There is no common scheme. The situation for the student is actually worse than this, since in no one university are all the points of view properly represented. Thus, a certain bias is inevitable. The main objection to the graduate school, however, as I have already pointed out, is that the science of human nature is not taught there. For this reason one usually advises a promising student to go to medical school, since this is the path to psychoanalysis, the man-wise science of today. Though this seems to be the best available program of education, it is by no means satisfactory.

In the first place, such a course is unnecessarily long and expensive for a student. It is unnecessarily long, because at least four of the nine years of preparation are spent in acquiring information which in his later work as a psychologist he will never need. Even if he wishes to become a psychiatrist a rudimentary knowledge of medicine is sufficient. For he will always refer patients with organic disease to a physician, just as a physician always refers patients with acute abdominal conditions to a surgeon.

Another argument against attending medical school is that the attitude of medical faculties is usually destructive to those who would understand the influence of the psyche on the body. The somewhat scornful complacency of the average medical man has been pointed out by Freud:

> If medical training would only deny information to the student in the field of neurosis, this would be tolerable. But medical training is doing more. It implants into the young student an incorrect and harmful point of view. Physi-

cians, whose interest for psychological facts has not been awakened, have naturally a tendency of making little of such facts, going even so far as to decry them as unscientific. Conditions of neurotic character are hardly ever taken seriously by them while their lack of knowledge serves to breed disrespect for psychological research.

Furthermore, the emphasis on a rigorous attention to physical signs and the mechanistic attitude which this engenders are inimical to the refinement of those functions of the mind which are primarily employed in making psychologic diagnoses. Psychologic intuition is a complicated process which cannot be discussed at the moment. Suffice it to say that it is not sharpened by assuming the wholly detached, systematically observing attitude of the physical scientist. Since this is a fact which most physicians have not been trained to appreciate, they do not realize how their instruction may dull the apperceptive powers of the student.

Finally, and this is the weightiest argument, the medical school does not provide courses in normal psychology or in psychologic observation and experimentation. As a result a medical graduate who takes up psychoanalysis has no adequate standard of critical judgment to guide. The standards which he was taught to use in dealing with physical disease are insufficient. And so, like some accomplished physicists who become childishly uncritical when they begin speculating about religion, many young physicians lose their heads when they have to deal with psychologic phenomena. There is no other explanation of why so many well trained medical students close their eyes with such docility and swallow the assertions of psychoanalysis bait, hook and sinker.

A final difficulty which confronts the would-be student of psychoanalysis is that there are at least four entirely incompatible schools of psychoanalysis, and although at the moment the freudian school is the most popular and the best organized for instruction and propaganda, its utter disregard of the findings and reflections of the other leading analysts is symptomatic of ominous myopia. Thus, the psychoanalyst is likely to be as limited in vision as the academic psychologist.

At present, then, there is no satisfactory solution of the problem for a young man who wants to acquire a well rounded education in a reasonably short time. Academic psychologists are looking critically at the wrong things. Psychoanalysts are looking with reeling brains at the right things. A student who really wants to obtain understanding can follow neither; other sciences can base their assumptions on the work of neither; the public can rely on neither. The average student, however, chooses, because he must, one school or the other, and so his intellectual development in the end becomes boxed in by circumstance. For even if he is clear-headed enough to perceive that the group with which he has been forced to cast his lot is shamelessly prejudiced, he knows

that bread is the staff of life and that he who sides with all men or with none goes hungry. The crucial time arrives. He hears the growling of his stomach, and his convictions are settled. The larger outlook fades. Thus, the existing social and institutional situation is destined to produce an even greater number of encrusted specialists.

In view of the potential importance of psychology, the existing Babel of authoritative voices, the confusion of those who wish to learn and, finally, the increasing demand for trained psychologists in every branch of social life, is it not desirable that some great university should establish a school of psychology—a school in which young men and women can be adequately trained? Such a school, let me say, would offer, as does the medical school, a four year course of instruction. It would require for admission certain preliminary studies—physics or chemistry, biology, elementary psychology and a phase of the history of culture—anthropology or sociology. The first year would be devoted to scientific method, general physiology, neuro-anatomy and neurophysiology, with special emphasis on the autonomic nervous system, followed by courses in general psychology, sensory psychology, animal psychology and the developmental and educational psychology of the child. The psychology of personality would be stressed, and the student would be given a thorough grounding in experimental methodology. In the third year there would be courses in psychopathology and psychoanalysis, supplemented by an elementary course in clinical medicine. The principles of psychotherapy and the analytic procedure would be taught. Such a school would necessarily maintain affiliations with a number of institutions in which practical instruction would be offered—an orphanage, a progressive school for problem children, a clinic for child guidance, clinics for the treatment of the neuroses and institutions for feebleminded, delinquent and psychotic patients. Finally, since a physiologic orientation tends to minimize social factors, courses in social psychology, sociology and the psychology of art, religion and science would be included. Nothing less than this can be counted on to prepare responsible men and women for research or for practice. The students who intended to practice psychoanalysis would take postgraduate courses and a year's internship in a hospital for patients with mental disease. For such students a didactic analysis, offered at a moderate cost, would be one of the requirements.

This, in brief, is a plan for establishing the study of man on a sound foundation. The details, naturally, must be carefully worked out and the funds must be provided, but the plan presents no inherent difficulties. Indeed, universities can immediately begin to work toward such an ideal by inaugurating certain changes. The following changes seem of greatest importance: (1) the enlargement and strengthening of psychology in the graduate school by inclusion of representative courses

from each special field, which would mean for most universities the development of a psychology of human motivation and the addition of courses in child psychology, psychopathology and clinical psychotherapy; (2) the bringing about of a reorientation of the special fields within the department, so that the psychology of motivation and development comes to occupy a primary and central position; (3) an increase in the number of courses, particularly of the practical or clinical courses, which must be completed before a degree of Doctor of Philosophy is awarded; (4) the establishment of closer relations with the allied disciplines, such as physiology, sociology and anthropology.

Since many of these developments have already taken place in several universities, it is not necessary to argue at length about their feasibility. One measure, however, the admission of practitioners to the college faculty, because of its importance and its novelty, deserves special consideration.

The inclusion of psychotherapeutists as members of the department is, I believe, essential, because an adequate science cannot be developed without the inclusion of phenomena which only psychotherapeutists are in a position to observe.

The science of psychology cannot prosper without the therapeutist, because in order to know human personality in its deeper and more deterministic aspects man not only must maintain an intimate association with many individual subjects over a period of months or of years but during this time must relentlessly pursue an analytic procedure which is harrowing, exacting and time-consuming to the subject. The analytic procedure is harrowing to the subject because it is directed toward the exposure of those carefully shrouded, haunting memories the recollection of which is so humiliating as well as toward the illumination of those twilight fantasies which go to make up that highly valued, solemnly secret mythology which holds sway over the subterranean regions of every mind. Since no man or woman sacrifices his or her inviolateness and endures the tedious tribulations of a prolonged analysis without the expectation of deriving benefit from it and since, by definition, the only persons who have dedicated their lives to the office of serving human beings in this capacity are the psychotherapeutists, it is they, and only they, who have the opportunity to observe directly the underlying forces of personality.

The psychotherapeutist, again, is the man who is specially trained in the method of establishing rapport and of unearthing by stages the deeper strata of the mind. In this realm, art and technic are everything, for a relationship of peculiar intimacy and trust must be established between the observer and the observed. Since it has been shown, moreover, that the subject is unconscious of the factors which determine the more intense experiences of life, a special technic must be employed

to bring them objectively into play, and only the psychotherapeutist is practiced in this technic.

Furthermore, the psychotherapeutist is by definition the only man who has a first-hand acquaintance with the phenomena of abnormal psychology, and the natural dissections of the mind that occur under such conditions are of signal import to an understanding of the normal personality. This is so because a preliminary analysis of an event into its functional parts is necessary to a complete description of anything whatsoever and because, whereas in harmonious personalities the parts of the psychic process are so merged that they are difficult or impossible to identify, in discordant and obsessed persons the existing conflict which is at the root of the trouble produces an analysis or a disbalance by which certain elements or processes present themselves in striking relief. If there are added to this natural analysis the process of disjunction which often occurs and that of dissociation by hypnosis which is occasionally resorted to in the course of treatment, it must be apparent that the psychotherapeutist comes into direct possession of elementary facts which do not fall within the experience of others.

Finally, the psychotherapeutist enjoys a unique position as an experimentalist. For every case is in truth an experiment, and within the limits of humane principles the psychologist may and should attempt various procedures with the purpose of modifying the existing structure and, in the rôle of catalyst, of bringing about the formation of new psychologic integrations. This aspect of the situation accords with the operational theory of knowledge, as set forth by Bridgman and Dewey, by which knowledge itself becomes a mode of practical action conforming to the experimental model. Instrumentalism in psychology refers to the procedures of analysis (deconditioning) and synthesis (conditioning), which are the means whereby a therapeutist attempts to change and control his subject. From this point of view, personality is not understood until the consequences of a consciously instituted procedure may be predicted and the prediction verified. For the ultimate aim in science is prediction and control, and so far as this is ever to be accomplished in the realm of personality it will be with methods devised by men who dedicate their wits to this particular task. In this respect the physician is the arch pragmatist and the sole counterpart of the analytic and synthetic chemist. In other words, he is the true experimentalist in the domain of human psychology.

To include psychotherapeutists in the faculty is to admit psychoanalysis to the university, simply because nowadays every first-rate therapeutist uses the technic or the theories of psychoanalysis in one form or another. A therapeutist appointed to the staff should be fully trained in freudian analysis and versed in the views of other leading analysts. A critical liberality in these matters is essential, for no modern

school of psychology can afford to neglect the distinguished contributions of such men as Jung and Rank.

Oddly enough the most determined opposition to the assimilation of psychoanalysis by academic psychology will probably come from the freudian analysts themselves. Their resistance will arise not so much from the shrewd suspicion that ideas are taken to universities to perish—or, if not to perish, to be bleached of their vitality—but from a certain fanatical determination to oppose any modification of the doctrine which Freud has created. This setting themselves apart from all other psychologic movements is the result of a variety of factors.

The hostility of traditional medicine has forced them to the extremity of a Ghetto ideology; an unholy reverence for Freud's genius has made them regard his critics as vicious enemies; a subjectively determined preoccupation with rudimentary erotic phenomena has blinded them to other obvious factors, and, finally, an utter lack of appreciation of the aim of science—the arrival at a common basis—has allowed them to remain eccentric and fractious. In short, with a few notable exceptions, freudians, though they emphatically pretend to a scientific attitude, are propelled by sentimental and religious motives, and hence it is possible to converse with them only within the narrow limits of their own conceptual framework.

If it were necessary, however, to choose between psychoanalysis and its opponents, one should, I think, without hesitation choose psychoanalysis, because, as compared with other schools, it is the most honest and unflinching in its investigation of many important, though commonly ignored, aspects of life and because it offers the best technic and the most suggestive theories for the immediate future. It bears enough fertility to change the march of history.

Personally, I believe that psychoanalysis needs the university. To the present time, it has been the creation of private practitioners—men who are prey to the claims of the nervous world. But now it has reached a stage at which it will benefit by companionship with academic psychology. Its concepts need to be exposed to the experimental method and to a rigorous criticism, and for this the men who carry on the work must be free to enjoy the kind of leisure and the intellectual fellowship which it is the business of a university to provide. Psychopathology must find contact with other schools of psychology, for just as pathology has come to rest on physiology, so must psychopathology finally establish itself on normal psychology.

I have laid such stress on prevailing discords that the reader may legitimately ask: How can a harmonious faculty of psychology be formed from such heterogeneous elements? Without a common terminology how will communication be possible? It will be difficult; one must acknowledge that from the outset. But the conditions are not, in

truth, as bad as I have painted them. For when I described the conflicts of opinion I was regarding each school as a joint stock company, and as joint stock companies men appear more congealed and indoctrinated than they do as individuals. Certainly in every group there are men of constructive intelligence to be found who, because they have enjoyed a scientific training and some living in the world, are capable of thinking beyond the theories with which they are officially affiliated. If such men are brought together there will certainly be disagreements about theoretical principles. But is this not true of all faculties? Within limits is it not, indeed, desirable—the inevitable condition for progressive development?

One can hardly suppose that in the beginning the faculty of a school such as I have proposed will be a strong one. Probably there are not enough psychologists and analysts now available to constitute a formidable company of scholars. But one may hope, on the basis of past experience, that from the best graduates of the new school a distinguished faculty will eventually be formed.

If a university waits until a conceptual scheme which all schools can accept has been constructed, the advancement of psychology will be indefinitely postponed. Until the conditions are created wherein students can acquire a first-hand acquaintance with the complete range of facts on which such a scheme must rest, all reflection is likely to be partial and inconclusive. A personal acquaintance with the facts is essential because, in psychology especially, second-hand facts are no longer facts. They have already undergone interpretation; that is, they have been assimilated to categories, and, as it happens, these are usually incommensurate with other categories.

It seems better, then, to start a school for the purpose of arriving at a unified system of ideas than to wait for the generation of ideas on which to found a school. The two factors, of course, are mutually dependent. But the creation of a theory depends on genius—something which no university can manufacture—whereas the conditions under which genius thrives are at least partially controllable. The establishment of a unifying theory would be the noblest aim that a school of psychology could set itself. This is right by all standards of elevated judgment, even though the average American may not readily agree to it. In this country, indeed, most people are even blind to the great practicality of a good theory; how, like a microscope, it centers attention on fundamental relations; how, by creating new symbols, it facilitates thought and communication; how it initiates more research, and hence the discovery of new facts. Perhaps it is not too fanciful to suggest that this emotionally sick world is in urgent need of a workable theory of personality. To be sure, the majority are no more aware of this need than certain physical sufferers of former times were aware that there

could be no sufficient alleviation of misery such as theirs until the atomic theory had been formulated.

The end of my reflection is this: Assemble the ablest representatives of each branch of psychology; give them facilities for research, opportunities for discourse and leisure for speculation. And as surely as clouds eventually disperse and expose the sun, the introspectionists will be forced out of their culdesac; the behaviorists will relinquish their juvenile metaphysics; the gestalt psychologists will be drawn into the field of motivation, and the psychoanalysts will be compelled to define their concepts and to think clearly. Thus a true school might come into being in which young men and women could learn what there was to know about man—the object which in all nature does and should concern them most.

In advocating the encouragement of psychologic science I have accepted pure knowledge as an unanalyzable satisfaction to the understanding—an ultimate value—and hence a sufficient goal for the dedication of one's best energies. But in valuating the proposed plan one should not fail to consider the probability of even greater secondary gains following in the wake of truth. For, since psychology deals directly with aspects of reality which are intimately bound up with human happiness, the most impartially collected facts will often suggest new and better modes, or new and better directions, of behavior. Thus, the advancement of the science will necessarily have a beneficial influence on practical action—the education of youth, the management of asocial persons, the treatment of disease, the constitution of new social patterns. And, most important of all, psychology will inevitably play a decisive rôle in shaping and accrediting the ideologies which are to come, the speculative outlooks which will clear the path and provide a form for personal development and the creation of enduring and of emergent synergies—erotic and communal. Psychology will have a hand in this, because the intelligences of the future will demand, so deeply has science implanted itself in the soil of man's imagination, that an ideology which shapes behavior be grounded on experience; that the possibility of its realization at least be suggested by the known facts and accepted theories of psychology. At present psychology is up to its head trying to ascertain the facts. It is too uncertain of itself to contribute anything to an ideology. But another time will come. For wisdom—that is, usable truth—is the secret aim of psychology.

Such presentiments of promise may be vague and illusory, but the present occasion is not. The present occasion is clear. The great tide, today and tomorrow, belongs to psychology. No university can afford to lose it, and, if it is to maintain its prestige, no university can fail to contribute to it.

THE PSYCHOGALVANIC REFLEX

APPLICATIONS TO NEUROLOGY AND PSYCHIATRY

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Approximately a thousand articles have appeared in medical and psychologic journals within the past forty years on the subject of the psychogalvanic reflex. Until recently the fact that the resistance of the human skin to the passage of imperceptible electric currents was decreased following certain psychic stimuli was looked on as an important objective means of measuring emotion, and many investigators advocated the use of this phenomenon in the study of the neuroses and the major psychoses. Unfortunately, earlier investigators were handicapped by a lack of knowledge concerning the physics and physiology of the reflex, the result being that experiments were usually poorly controlled and the findings of different workers were often contradictory. Landis [1] stressed the chaotic state of the literature in this field and concluded that "there is no good and sufficient reason, except that of historical fallacy, why one should continue to hold that the 'psychogalvanic reflex' has anything to do with nervous and mental diseases as such."

However, much progress has been made in recent years. The use of modern electrical apparatus has resulted in a virtual solution of the physical problem involved. Emphasis on animal experimentation has brought about a more thorough understanding of the physiology of the reflex, and it has become clear why so much of the past work in this field has been valueless. On the other hand, justifiable applications now become logically indicated. A complete but uncritical review of the literature on the subject was given by Landis.[2]

Read at the meeting of the Boston Society of Psychiatry and Neurology, Feb. 21, 1935.

From the Neurological Unit, Boston City Hospital, and the Department of Neurology, Harvard Medical School.

1. Landis, Carney: Psychiatry and the "Psychogalvanic Reflex," Psychiatric Quart. **6**:262, 1932.

2. Landis, Carney, and DeWick, H. N.: The Electrical Phenomena of the Skin (Psychogalvanic Reflex), Psychol. Bull. **26**:64, 1929. Landis, Carney: Electrical Phenomena of the Skin, ibid. **29**:693, 1932.

THE NATURE OF THE PSYCHOGALVANIC REFLEX

The Physics of the Psychogalvanic Reflex.—Two methods may be used for eliciting the reflex. In the Féré [3] phenomenon the psychogalvanic reflex is an apparent decrease in the resistance when a small external direct current is being passed through the body. Gildemeister [4] showed that the resistance as so measured is not the "true resistance," which can be measured by using alternating currents, but represents chiefly a polarization phenomenon or production of "back E M F." In the Tarchanoff [5] phenomenon no external current is used. Electrodes are attached to different parts of the body and placed in circuit with a sensitive galvanometer. A spontaneous current is generated by the body and causes a deflection in the galvanometer. The psychogalvanic reflex is a change in this deflection following certain stimuli. The same polarization phenomenon is responsible for the psychogalvanic reflex in either method.

It has been demonstrated that the results of different workers are not comparable unless the following are taken into account: the strength of the external current, the characteristics of the circuit used (if a Wheatstone bridge is used, values of the various resistances must also be given), the area and composition of the electrodes and the concentration and temperature of any solutions used.[6]

McClendon and Hemingway [7] showed that the polarization which occurs during the psychogalvanic reflex is caused by changes in the capacity of the electrical double-layer which surrounds individual cells. This is equivalent to changes in the permeability of the cell membrane, which may be looked on as fundamental in the psychogalvanic reflex.

The Physiology of the Psychogalvanic Reflex.—It is known that the electrical resistance is localized almost entirely in the skin. If a pinprick is made through the skin under an electrode, the resistance drops practically to zero.[8] The skin over the various parts of the body differs in

3. Féré, C.: Note sur des modifications de la tension électrique dans le corps humain, Compt. rend. Soc. de biol. **5**:28, 1888.

4. Gildemeister, M.: Ueber die physikalisch-chemischen und physiologischen Vorgänge im menschlichen Körper auf denen der psychogalvanischen Reflex beruht, München. med. Wchnschr. **60**:2389, 1913.

5. Tarchanoff, J.: Ueber die galvanischen Erscheinungen an der Haut des Menschen bei Reizung der Sinnesorgane und bei verschiedenen Formen der psychischen Tätigkeit, Arch. f. d. ges. Physiol. **46**:46, 1890.

6. James, H. E. O., and Thouless, R. H.: A Note on the Effect of Polarization in Psycho-Galvanic Experiments, Brit. J. Psychol. **17**:49, 1926. Forbes, T. W., and Landis, Carney: A Systematic Investigation of Methodology in the Measurement of Electrical Phenomena of the Skin, Psychol. Bull. **29**:675, 1932.

7. McClendon, J. F., and Hemingway, A.: The Psychogalvanic Reflex as Related to the Polarization-Capacity of the Skin, Am. J. Physiol. **94**:77, 1930.

8. Farmer, E., and Chambers, E. G.: Concerning the Use of the Psychogalvanic Reflex in Psychological Experiments, Brit. J. Psychol. **15**:237, 1924.

its electrical properties.[9] Only over the palms and soles is the psychogalvanic reflex easily elicited. The electrical properties of the dorsum of the hand are independent of those of the palm.[10] Changes in these two regions may take place in opposite directions,[11] so that the practice of using a finger immersed in a solution as an electrode may be misleading. The palmar electrical changes, including the psychogalvanic reflex, are known to be associated with the activity of the sweat glands.[12] The electrical properties of the dorsum depend on the layer of epithelial cells.[10] The circulation has been ruled out as not affecting either.[13]

While the sweat glands are intimately bound up with the psychogalvanic reflex, it is not the secretion or the presence of the perspiration itself or the action currents in the sweat glands [14] that cause the reflex. Changes in permeability of the cell membranes of the sweat glands produce the electrical effects on which the reflex depends.[15] These changes in permeability are brought about through the sympathetic nervous system, which abundantly supplies the sweat glands.[16] The intact sympathetic nerve supply to the skin under the electrode is a necessary and sufficient condition for the production of the psychogalvanic reflex following an appropriate stimulus.[17]

The sensory arm of the reflex may be any sensory stimulus, usually tactile, auditory or visual, although olfactory and gustatory stimuli have been used.[5] The impulses travel along the usual sensory pathways to the brain.[18] Since the psychogalvanic reflex can be elicited in decorticated

9. Leva, J.: Ueber einige körperliche Begleiterscheinungen psychischer Vorgänge, mit besonderer Berücksichtigung des psychogalvanischen Reflexphänomens, München. med. Wchnschr. **60**:2386, 1913.

10. Richter, C. P.: Physiological Factors Involved in the Electrical Resistance of the Skin. Am. J. Physiol. **88**:596, 1929.

11. Levine, Maurice: Measurement of Electrical Skin Resistance, Arch. Neurol. & Psychiat. **29**:828 (April) 1933.

12. Darrow, C. W.: The Electrical, Circulatory, Secretory, and Thermal Reflexes of the Skin, Proc. Internat. Cong. Psychol. **9**:136, 1929.

13. Darrow, C. W.: The Galvanic Skin Reflex, not a Vasoconstrictor Phenomenon, Psychol. Bull. **26**:155, 1929.

14. Gildemeister, M.: Die Elektrizitätserzeugung der Haut und der Drüsen: D. Der galvanische Hautreflex, in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1928, vol. 8, pt. 2, p. 775.

15. McClendon and Hemingway.[7] Gildemeister.[14]

16. Gildemeister, M.: Der galvanische Hautreflex als Teilerscheinung eines allgemeinen autonomen Reflexes, Arch. f. d. ges. Physiol. **197**:432, 1922-1923.

17. Schilf, E., and Schuberth, A.: Ueber das sogenannte psychogalvanische Reflexphänomen beim Frosch und seine Beziehung zum vegetativen Nervensystem, Arch. f. d. ges. Physiol. **195**:75, 1922.

18. Foa, C., and Peserico, E.: Le vie del reflesso neuro-galvanico, Arch. di fisiol. **21**:119, 1923.

animals, a relay to the higher centers is not necessary for its production.[19] The center from which the motor sympathetic impulses arise lies in the floor of the third ventricle in close association with other vital centers.[20] This center can be stimulated by sensory impulses, as discussed, or directly through emotional stimuli arising in the cortex.[19] In the conscious animal a sensory stimulus may be reenforced by a concomitant emotional reaction, both acting on the hypothalamic center; or, in the absence of sensory stimuli, a spontaneous emotion may stimulate the center and cause a psychogalvanic reflex.

The motor arm of the reflex arises in the hypothalamic center and passes down the spinal cord along the usual sympathetic channels.[19] It leaves the cord in the white rami communicantes to join the chain of sympathetic ganglia, whence it supplies the sweat glands of the skin via the gray rami communicantes and the spinal nerves.[17]

What actually occurs at the sympathetic nerve endings on stimulation is unknown, but the result is a temporarily increased permeability of cell membranes in the immediate vicinity. There is reason to believe [21] that here, as elsewhere in the sympathetic nervous system, stimulation causes the secretion of a chemical substance, sympathin, which is responsible for the changes that occur. The accompanying illustration is a schematic representation of the psychogalvanic reflrex arc.

APPLICATIONS

The psychogalvanic reflex can be used as an indicator of activity in any one of its five divisions. It goes without saying that when attention is focused on any one division, every effort should be made to control the other divisions.

1. *Sensation.*—Levine and Wolff [22] used the psychogalvanic reflex in animals as an indicator of sensory perception. They were able to show that in cats under anesthesia induced by bulbocapnine and procaine the blood vessels of the pia are supplied with sensory nerves. Schwartz [23] in a similar manner demonstrated that reflex activity can exist solely

19. Langworthy, O. R., and Richter, C. P.: The Influence of Efferent Cerebral Pathways upon the Sympathetic Nervous System, Brain **53**:178, 1930.

20. (*a*) Foa and Peserico.[18] Langworthy and Richter.[19] (*b*) Wang, G. H.: Galvanic Skin Reflex and the Measurememnt of Emotion, Canton, China, Sun Yat Sen University Press, 1930.

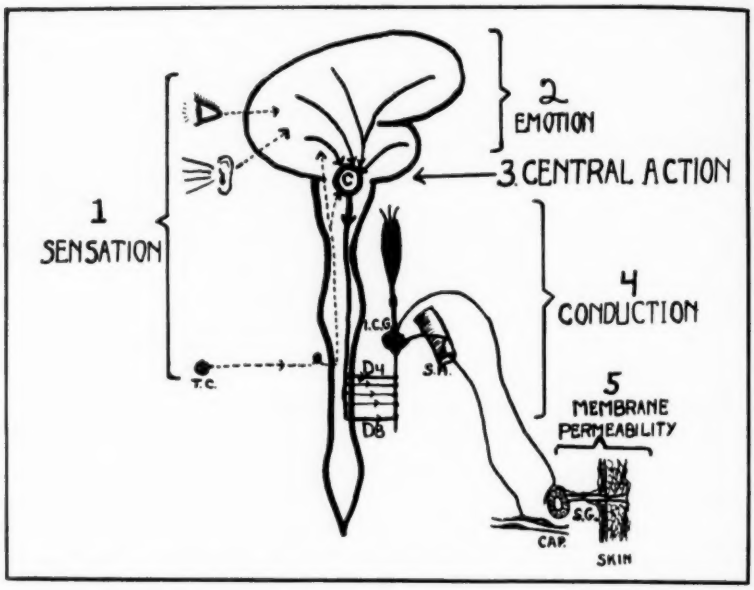
21. Solomon, Philip, and Tatel, Howard: Unpublished observations.

22. Levine, Maurice, and Wolff, H. G.: Cerebral Circulation: Afferent Impulses from the Blood Vessels of the Pia, Arch. Neurol. & Psychiat. **28**:140 (July) 1932.

23. Schwartz, H. G.: Reflex Activity Within the Sympathetic Nervous System, Am. J. Physiol. **109**:593, 1934.

within the sympathetic nervous system. Since the usual ways of observing the effects of sensory stimulation in animals, viz., outcry, overt activity, etc., are not reliable and, at best, are only roughly quantitative, the use of the psychogalvanic reflex seems admirably indicated for this purpose.

Some patients with hysterical manifestations may be likened to dumb animals with respect to the difficulty in communication of certain sensory perceptions. In an area of skin which is anesthetic because of a lesion of a peripheral nerve, stimulation with a pin fails to produce the psychogalvanic reflex.[24] If the anesthesia is on a hysterical basis,



Schematic representation of the psychogalvanic reflex arc. Sensory impulses (*1*) enter the central nervous system in the usual way and affect the hypothalamic center (*3*) either directly or through a relay in the higher centers (*2*). Spontaneous emotion may stimulate the hypothalmic center. The motor arm of the reflex (*4*) arises in the hypothalamic center, passes down the spinal cord along the usual sympathetic channels and leaves the cord in the white rami communicantes to join the chain of sympathetic ganglia, whence it supplies the sweat glands of the skin via the gray rami communicantes and the spinal nerves. Increased permeability of the membranes of the cells of the sweat glands (*5*) causes the electrical phenomenon known as the psychogalvanic reflex. *T. C.* indicates a tactile corpuscle; *C* indicates a hypothalamic center; *D4* and *D8* indicate the white rami communicantes from the fourth to the eighth dorsal vertebra; *I. C. G.* indicates an inferior cervical ganglion; *S. A.*, a subclavian artery; *CAP.*, a capillary, and *S. G.*, a sweat gland.

24. Richter, C. P.: Nervous Control of the Electrical Resistance of the Skin, Bull. Johns Hopkins Hosp. **45**:331, 1930.

the reflex occurs normally.[25] This situation has resulted in an effective test for differentiating between anesthesia due to hysteria and that due to a lesion of a peripheral nerve.[26] When the area of anesthesia is such that it suggests a transverse lesion of the spinal cord, the differentiation by means of the psychogalvanic reflex is not so clear. Richter [27] showed that in cats with a transected spinal cord recovery from shock is associated with the return of the psychogalvanic reflex in the paralyzed parts. While a center in the spinal cord is thus demonstrated in animals, there is a difference of opinion regarding the application of these results to man.[28] In the author's experience transection of the spinal cord resulted in abolition of the reflex in one patient for a period of sixteen months. It has therefore been concluded that the presence of the reflex on stimulation of the anesthetic skin of a patient with paraplegia is evidence in favor of the diagnosis of hysteria.

2. *Emotion.*—The application of the psychogalvanic reflex in the fields of psychology and psychiatry has been the chief cause of the confusion in the literature referred to previously. However, when it is remembered that highly integrated emotional or "psychic" stimuli from above affect the hypothalamic center in much the same manner as sensory stimuli from less complex levels, several legitimate applications become clear. Jung [29] was the first to use the reflex in connection with word association tests for unearthing deep-lying complexes. Prince and Peterson [30] used the reflex in a patient with multiple personalities and demonstrated that words which had an emotional connotation to personality C but were not significant to personality A nevertheless caused a strong psychogalvanic reflex in personality A. They concluded: "Memories of conscious experiences which the subject cannot consciously recall, i. e., for which he has amnesia, may be conserved and give rise to the same galvanic reactions which are obtained from conscious emotional states." In a similar way they showed that objects not consciously perceived by peripheral vision may be "co-consciously" perceived.

25. Levine, Maurice: Psychogalvanic Reaction to Painful Stimuli in Hypnotic and Hysterical Anaesthesia, Bull. Johns Hopkins Hosp. **46**:331, 1930.

26. Zimmern, A., and Logre, A.: Le réflexe galvano-psychique, J. de radiol. et d'électrol. **2**:610, 1916.

27. Richter, C. P.: Galvanic Skin Reflex from Animals with Complete Transection of the Spinal Cord, Am. J. Physiol. **93**:468,1930. Richter, C. P., and Shaw, M. B.: Complete Transections of the Spinal Cord at Different Levels: Their Effect on Sweating, Arch. Neurol. & Psychiat. **24**:1107 (Dec.) 1930.

28. Schilf and Schuberth.[17] Wang.[20b]

29. Jung, C. G.: On Psychophysical Relations of the Associative Experiment, J. Abnorm. Psychol. **1**:247, 1907.

30. Prince, Morton, and Peterson, Frederick: Experiments in Psychogalvanic Reactions from Co-Conscious (Subconscious) Ideas in a Case of Multiple Personality, J. Abnorm. Psychol. **3**:114, 1908.

Recently the psychogalvanic reflex has been used popularly as a "lie detector." The difficulty with this and similar applications lies in the fact that the reflex does not distinguish between different kinds of emotions. A strong reflex may be associated with a feeling of guilt, fear, shame or amusement. Attempts to use the reflex as an index of emotional reactivity [31] have been shown to be grossly misleading,[32] as can readily be understood when the physiology of the reflex is considered. A large reflex may mean a strong response in any one of the five divisions of the reflex arc.

The psychogalvanic reflex is being successfully used in the study of experimentally conditioned reflexes. Smith [33] has conditioned subjects to certain words by following them with a painful electric shock. By observing the resulting psychogalvanic reflex, which after a few repetitions follows the word without the shock, he has been able to determine the effects of various factors on the conditioned reflex and on the deconditioning process.

3. *Central Action.*—The clinical study of the sympathetic nervous system has been handicapped by the lack of a suitable indicator of sympathetic activity. That the electrical resistance of the skin is such an indicator has been demonstrated.[34] Stimulation of the sympathetic system uniformly causes a decrease in the electrical resistance over the palms and soles, while inhibition causes a rise. These changes are likely to be more prolonged under certain conditions than those seen in the psychogalvanic reflex, so that it is more proper in this respect to speak of changes in the level of the electrical resistance than of the reflex alone.

Richter [35] showed that the electrical resistance of the skin rises enormously during normal sleep and that the depth of the sleep is probably proportional to the height of the resistance. Awakening causes an instant drop in the resistance to the waking level. A method is therefore available for studying variations in the depth of normal sleep without awakening the subject. Thus far little use has been made of

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31. Farmer and Chambers.[8] Peterson, Frederick: The Galvanometer as a Measure of Emotions, Brit. M. J. **2**:804, 1907. Solomon, A. P., and Fentress, T. L.: Galvanic Skin Reflex and Blood Pressure Reactions in the Psychoneuroses, J. Nerv. & Ment. Dis. **80**:163, 1933. Syz, H. C., and Kinder, E. F.: Electrical Skin Resistance in Normal and in Psychotic Subjects, Arch. Neurol. & Psychiat. **19**:1026 (June) 1928.

32. Landis, Carney: Psychology and the Psycho-Galvanic Reflex, Psychol. Rev. **37**:381, 1930.

33. Smith, Karl: Personal communication to the author regarding unpublished data.

34. Gildemeister.[16] Schilf and Schubert.[17] Wang.[20b]

35. Richter, C. P.: The Significance of Changes in the Electrical Resistance of the Body During Sleep, Proc. Nat. Acad. Sc. **12**:214, 1926.

this possibility. Richter [36] showed that the sleep produced by various hypnotics is also accompanied by an inhibition of the sympathetic centers. The attacks of sleep in narcoleptic patients do not differ from normal sleep in this respect.[37] The value of drugs in narcolepsy may therefore be studied by this method.[38]

The use of the electrical resistance of the skin as a measure of sympathetic activity in various clinical conditions has hardly been commenced. Migraine and epilepsy are diseases frequently explained on the basis of autonomic dysfunction. The author is gathering evidence that in neither of these conditions do changes in the autonomic system play a part.

4. *Conduction.*—Since the interruption of the sympathetic supply to a part abolishes the psychogalvanic reflex to that part, the reflex can be used clinically when lesions of the sympathetic pathways are suspected. In a patient with a tumor of the neck Richter [39] showed that unilateral involvement of the sympathetic chain caused the disappearance of the reflex on the palm of the same side. In a patient who had been given an injection of alcohol the stellate ganglion on one side, I demonstrated that the reflex was absent on the palm of that side.

Tower and Richter [40] used the return of the psychogalvanic reflex after experimental section of different parts of the sympathetic chain as a criterion of regeneration. In this way they were able to study the process of repair within the sympathetic nervous system. It is probable that further experimental work along these lines will bring forth considerable valuable information regarding the functional anatomy of the sympathetic nervous system.

5. *Permeability of the Cell Membrane.*—The application of the electrical resistance method to the many problems involving the per-

36. Richter, C. P.: Sleep Produced by Hypnotics Studied by the Electrical Skin Resistance Method, J. Pharmacol. & Exper. Therap. **42**:4, 1931.

37. Richter, C. P.: Pathological Sleep and Similar Conditions Studied by the Electrical Skin Resistance Method, Arch. Neurol. & Psychiat. **21**:363, (Feb.) 1929.

38. An interesting point in this connection may be mentioned at the risk of digressing. It has been known since the time of Seneca that lightning spares the sleeper. To my knowledge no scientific explanation has ever been offered for this curious fact. Can it be that the increased electrical resistance of the skin associated with sleep is life saving to the person who is able to sleep through a lightning storm?

39. Richter, C. P.: A Study of the Electrical Skin Resistance and the Psychogalvanic Reflex in a Case of Unilateral Sweating, Brain **50**:216, 1927.

40. Tower, S. S., and Richter, C. P.: Injury and Repair Within the Sympathetic Nervous System: I. The Preganglionic Neurons, Arch. Neurol. & Psychiat. **26**:485 (Sept.) 1931; II. The Postganglionic Neurons, ibid. **28**:1139 (Nov.) 1932.

meability of cell membranes is almost entirely untouched. Ebbecke [41] and Gildemeister [42] made suggestions in this direction. The method is particularly applicable in the study of drugs. Here it is advisable to use the electrical resistance over the dorsum of the hand as an indicator, as the sympathetic effects are thereby largely ruled out. In working with the resistance of the dorsum of the hand, it must be noted that uniformly there is a marked diminution in resistance during the first half-hour or more of an experiment, after which a fairly constant level is reached. Therefore, drugs to be tested should not be given until after the fall has definitely stopped. The reason for this reduction is not clear, but it may be associated with the progressive permeation of the skin by the electrolyte.

DISCUSSION

DR. H. R. VIETS: Dr. Solomon has thrown light on the anatomy and physiology. It used to be thought that this reflex had some clinical application, and I believe that Golla wrote about its value in the differential diagnosis of hysteria and neurasthenia. Of course, with the development of newer methods this work is now of no particular value. It was, however, considerably discussed, particularly by English neurologists, just after the World War.

DR. H. H. MERRITT: There has been much popular talk with regard to the use of this instrument as a lie detector. Can Dr. Solomon tell if the psychogalvanic reflex is of any value in the detection of falsehoods?

DR. M. FREMONT-SMITH: I wish to ask if in any given person the psychogalvanic reflex was constant. Would it be possible to study a patient with a certain psychogalvanic reflex, psychoanalyze him and then see whether one could find a change in the reflex which might be used as a criterion of lessened basal affect?

DR. I. CORIAT: Several years ago I was greatly interested in experiments on the association tests, particularly when the so-called complex indicator was used. Under the latter conditions the psychogalvanic reflex was more marked than after indifferent words. It could be demonstrated that events, words, situations, etc., of which the patient was unaware, for which the patient was amnesic or which he had repressed could produce the same reflex reaction as those of which the patient was aware.

DR. KARL M. BOWMAN: Dr. Solomon spoke of there being different reactions in the palm and back of the hand. Can this explain why some investigators have had such poor results with the psychogalvanic reflex? I saw a patient in 1915 who was supposed to have burned down the hospital gymnasium; he denied having done so. He was given Jung's word association test together with a measurement of the psychogalvanic reflex. No reactions were elicited. About two years later he was caught by the police setting two fires and was returned to the hospital. He then admitted having set fire to the gymnasium. In this case the

41. Ebbecke, U.: Die lokale galvanische Reaktion der Haut (Ueber die Beziehung zwischen lokaler Reizung und elektrischer Leitfähigkeit, Arch. f. d. ges. Physiol. **190**:230, 1921.

42. Gildemeister, M.: Ueber elektrischen Widerstand, Kapazität, und Polarisation der Haut, Arch. f. d. ges. Physiol. **175**:84, 1919.

entire hand was immersed. If I understand Dr. Solomon correctly, that might have interfered with any satisfactory readings from the psychogalvanic reflex.

DR. HENRY SCHWARTZ: Can the psychogalvanic reflex be elicited in a decorticated animal?

DR. PHILIP SOLOMON: In the limited time it was impossible to mention every investigator who has worked with the psychogalvanic reflex. Golla attempted to use the reflex in psychologic problems. It is in such applications that the findings of different works are so often contradictory. Landis, in discussing the literature on this phase of the subject, concluded: "There is no good and sufficient reason, except that of historical fallacy, why one should continue to hold that the 'psychogalvanic reflex' has anything to do with nervous and mental diseases as such."

The difficulty with using the reflex as a lie detector rests in the fact that the reflex does not distinguish between different kinds of emotion. A strong psychogalvanic reflex may be associated with a feeling of guilt, fear, shame or amusement. Besides, every now and then persons who seem to be normal in every other way have no psychogalvanic reflex. This probably was the case with Dr. Bowman's patient, although it may well be that improved apparatus and technic would have brought out a reflex.

In reply to Dr. Fremont-Smith's question, I should say that the magnitude of the psychogalvanic reflex is too variable in any individual person to warrant its use as a criterion of effect following psychoanalysis or other therapy. It may be that it could be so used with respect to a single complex or stimulus word if the proper precautions were taken to control the experiment. Dr. Karl Smith at Harvard is interested at present in the question of applying the psychogalvanic reflex to problems in psychoanalysis.

In answer to Dr. Schwartz, I have done very little experimentation on animals. Langworthy and Richter have elicited the psychogalvanic reflex in decorticated animals. It is true that under these circumstances "psychogalvanic reflex" is hardly an accurate name, as Gildemeister has recently pointed out. The name has the virtue, however, that most persons know what is meant when it is used.

Clinical Notes

DIABETES INSIPIDUS AND FRÖHLICH'S SYNDROME ASSOCIATED WITH ENCEPHALITIS OF THE HYPOTHALAMIC REGION

ROBERT A. MOORE, M.D., AND E. H. CUSHING, M.D., CLEVELAND

Despite reports of over 100 cases of diabetes insipidus with autopsy observations in the literature and the large number of experimental investigations which have been undertaken to elucidate the location of the center controlling water balance, there is confusion concerning the exact pathologic anatomy and physiology of this disease.

REPORT OF A CASE

History.—A white man, a Hungarian Jew, was first admitted to the Lakeside Hospital on Aug. 25, 1930, two years before his death, to the service of one of us (E. H. C.). Dr. C. S. Beck and Dr. J. M. Hayman Jr. supplied the following clinical details. For five months preceding his admission the patient complained of polydypsia and polyuria. He had had nocturia, urinating two or three times nightly for years. The appetite had been good, and there had been a loss of less than 10 pounds (4.5 Kg.) in weight. Shortly before admission to the hospital he had suffered from severe constipation. There had been absence of libido for four years. The patient drank coffee and smoked, but rarely used alcohol and said that he had never had a venereal infection. Occasional headaches and short attacks of dizziness had occurred during the month preceding admission. The only therapy previous to admission was the administration of hydrochloric acid three times a day.

Examination.—Physical examination gave negative results except for incidental findings of carious teeth and large tonsils. There was a definite suggestion of Fröhlich's syndrome at this time. Vision was normal, and examination of the eyegrounds gave negative results. The blood pressure averaged 135 systolic and 90 diastolic.

Laboratory Examination.—The specific gravity of the urine was 1.001, and there was no albumin or sugar. Microscopically, the urine was normal. Examination of the blood gave the following results: red cells, 4,820,000; white cells, 12,400; hemoglobin, 88 per cent; differential count, normal; urea, 30.5 mg., and sugar, 98 mg. Examination of the spinal fluid revealed normal dynamics and an initial pressure of 162 mm. of water. Compression of the right jugular vein raised the pressure to 220 mm. and of the left jugular vein to 340 mm. There were 8 cells per cubic millimeter and 100 per cent lymphocytes. The Wassermann reaction was negative; the colloidal gold curve, 1112220000; the Pandy test, negative, and the test for sugar, positive. Examination of the stools gave negative results. The basal metabolic rate was normal. Tests of renal function gave normal results. An attempt was made to control thirst by increasing the amount of saliva by the use of pilocarpine and by painting the nasopharynx with a solu-

From the Institute of Pathology and the Department of Medicine, Western Reserve University and the Lakeside Hospital.

Presented at a meeting of the Cleveland Neurological Society on Nov. 9, 1932, and at a meeting of the Midwestern Neuro-Psychiatric Association in October 1933.

tion of cocaine. Neither of these measures resulted in any significant change in the amount of fluid intake or output.

Course.—During a subsequent period of fourteen days in the hospital in October 1930 no additional pertinent facts were elicited. Twenty-two months later, on Aug. 11, 1932, the patient was readmitted with the complaint of attacks during which "things turned black" and there were accompanying diplopia, failure of vision, dizziness and weakness. A roentgen treatment to the region of the sella turcica six months before admission reduced the output of urine from 15 to 5 or 6 liters a day. The dizziness was most marked when the output was highest. The hair did not grow as rapidly as formerly. Examination revealed a distribution of fat and hair of the neutral type, with a tendency more to the feminine type. The

Fig. 1.—Gross photograph of the base of the brain showing swollen optic nerves, chiasm and tracts.

left pupil was slightly larger than the right; both were irregular and did not respond to light but responded in accommodation. There was no photophobia or nystagmus. Convergence was poor, with double vision for objects closer than 14 cm. The optic disks were pale but well defined, except in the upper nasal quadrant of the left disk. There was an area of black pigmentation around the disks. The visual fields were uniformly reduced, with slight bitemporal hemianopia. Special examination for the integrity of the cranial nerves revealed no abnormality except in the optic nerve and ocular convergence as already noted. The sensory and proprioceptive senses were normal, and muscular activity was intact. Laboratory examination gave negative results except for a moderate anemia. Because of the rapid failure of vision, Drs. E. C. Cutler and C. S. Beck advised surgical exploration of the middle cranial fossa, giving a probable diagnosis of

suprasellar cyst. Roentgen examination of the region of the sella turcica gave negative results.

Operation.—Exploration through a large frontoparietotemporal bone flap on the left side revealed a few dural-arachnoid adhesions over the left frontal lobe and enlargement of the optic nerves and chiasm. Needle puncture of the pituitary gland revealed only a few drops of yellow fluid. The sheath of the optic nerves was incised, and the flap was closed. The postoperative course was stormy, and death occurred on the seventh postoperative day without recovery of consciousness. A few days before death there were marked hyperpnea and moderate cyanosis.

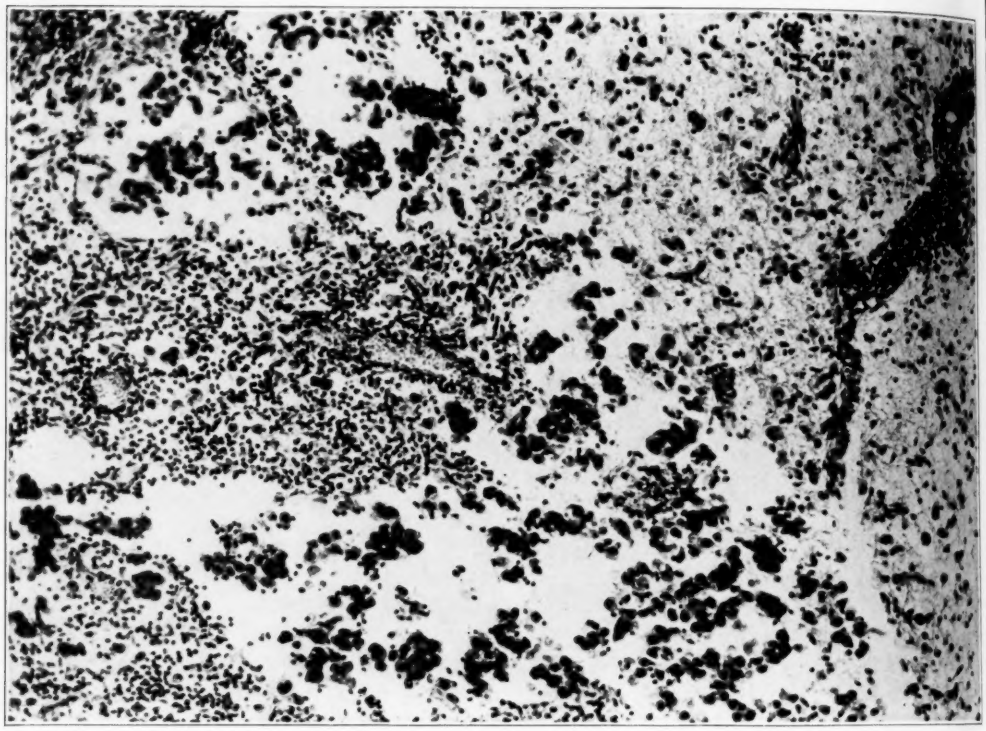

Fig. 2.—A section from the hypothalamic region. On the right is edematous brain tissue with diffuse and perivascular lymphocytic infiltration. On the left there is more extensive degeneration with necrosis of small areas. Reduced from a magnification of × 110.

At that time the carbon dioxide-combining power of the blood was 16.6 volumes per cent.

Autopsy.—This was performed by one of us (R. A. M.) twenty-one hours after death and was limited to the brain and kidneys. The kidneys showed no gross or microscopic change, and the glomerular count by Dr. Hayman was 1,288,000, a normal value. The surgical wound showed slight healing and was free from infection. There was a moderate amount of clotted blood in the extradural space on the left side. The external appearance of the brain was not remarkable, except for the chiasmal and hypothalamic regions. The pituitary gland was grossly

normal. The optic nerves, chiasm and tracts were enlarged, soft and red. Section of these structures revealed the same type of change. The remainder of the brain on section showed no pathologic change other than a small cyst in the left lenticular nucleus and two small hemorrhages in the same region.

Microscopically, as shown in figure 2, there was extensive degeneration and exudation in the hypothalamus and optic chiasm. This was characterized by perivascular infiltration with lymphocytes, hyperemia and degeneration of focal areas of the hypothalamus and chiasm, with infiltration into these areas of lymphocytes and atypical compound fat granule cells. As far as can be determined in the sections available, all of the nuclei of the hypothalamus, that is, the nucleus tuberis, the nucleus paraventricularis and the nucleus supra-opticus on both sides were completely destroyed. Material was not available for a study of the possible degeneration of tracts between these structures and the posterior lobe of the pituitary gland. The lesion in the chiasm was of a similar nature and extended for a short distance into both optic nerves and tracts. In addition to the lesion within the nerve there were extensive lymphocytic infiltration in the pia-arachnoid and some slight evidence of fibroblastic proliferation. Sections of other portions of the brain revealed no pathologic change. The pituitary showed no microscopic abnormality.

COMMENT

The problems presented by this case are as follows: 1. Clinically, there were definite pituitary-controllable diabetes insipidus, a moderately well defined Fröhlich syndrome and a disease of the optic nerves which produced marked constriction of both visual fields with a tendency to bitemporal hemianopia. 2. Physiologically, there was apparent dysfunction of the pituitary secretion. 3. Pathologically, there were extensive encephalitis of the entire hypothalamus and severe degeneration and inflammation of the optic nerves, chiasm and tracts with a morphologically intact pituitary gland.

In an analysis of 107 cases of diabetes insipidus, Fink,[1] found 68 due to tumor (63 per cent), 14 due to syphilitic disease (13 per cent), 5 due to tuberculosis and 9 due to nonspecific inflammatory disease. In the majority of instances the disease was so extensive that definite localization was impossible. In 14 of 39 cases of extrapituitary disease there was specific mention that the hypophysis was normal. On the contrary, there were 25 cases in which the posterior lobe of the hypophysis was the only structure involved. The severe process in the hypothalamus with no demonstrable changes in the posterior lobe of the pituitary gland renders our case unsatisfactory for further analysis of this point. A considerable number of cases of diabetes insipidus following encephalitis has been reported in the past ten years, and it is possible that careful and exact studies of these may furnish additional information. Certainly in all such cases examinations should be made and the gross material fixed with a view to definite delineation of the hypothalamic nuclei and tracts. Warner [2] has shown that a lesion of the nucleus tuberis and the anterior hypothalamic nucleus produced polyuria in one dog. Further pathologic evidence on the problem was furnished by Eaves and Croll,[3]

1. Fink, E. B.: Diabetes Insipidus: Clinical Review and Analysis of Necropsy Reports, Arch. Path. **6**:102 (July) 1928.

2. Warner, F. J.: The Histopathology of Experimental Diabetes Insipidus, J. Nerv. & Ment. Dis. **73**:375, 1931.

3. Eaves, E. C., and Croll, M. M.: Pituitary and Hypothalamic Region in Chronic Epidemic Encephalitis, Brain **53**:56, 1930.

who found that a slight postencephalitic lesion of the hypothalamus may produce diabetes insipidus but that a severe lesion does not do so. They explained this on the basis that the hypothalamus exerts an inhibitory effect on the pituitary gland which is accentuated in a slight lesion but is destroyed by a severe lesion. Simmonds [4] found a case of metastatic carcinoma of the posterior lobe with polyuria, which later disappeared. This, with other evidence, has been taken to support the hypothesis that diabetes insipidus is the result of disease of the posterior lobe of the pituitary gland in the presence of a normal anterior lobe. The evidence from the standpoint of the morbid anatomist and experimental pathologist is that the pathologic lesions associated with diabetes insipidus are varied in character and distribution and that no single explanation is possible except on the basis of an as yet poorly understood pituitary-infundibular-hypothalamic complex, each structure operating separately or through the others.

The pathologist has no more definite information on the frequent association of Fröhlich's syndrome and disease of these structures. The same variety of processes have been described, and no evidence can be added from this case.

The ocular symptoms in this case, at least clinically, belong to the group described by Heuer and Vail [5] as the chiasmal syndrome. Cushing stated that such a syndrome may be due to meningioma, pituitary adenoma, cyst of Rathke's pouch, glioma of the chiasm or the hypothalamus, chronic local arachnoiditis, syphilitic meningitis or aneurysm. In the present case there appears to be no logical reason for the separation of the disease of the chiasm from that of the hypothalamus. The structures have abundant contiguity of tissue, and hence spread of an infection from one to the other is possible. The character of the histologic changes also supports the view that there is one disease entity. The arachnoiditis, stressed by Cushing, was far overshadowed in our case by the degenerative and exudative lesions in the nerve.

SUMMARY

A case of clinical diabetes insipidus, Fröhlich's syndrome and the chiasmal syndrome, with a degenerative and inflammatory lesion of the hypothalamus and optic chiasm and no pathologic change in the pituitary gland, is reported. The anatomic evidence indicates that these clinical syndromes are not related to a definite focal lesion of the hypothalamic-pituitary region, but rather that a change in one or more areas may give the same clinical picture.

4. Simmonds, G.: Zur Pathologie der Hypophyse, Verhandl. d. deutsch. path. Gesellsch. **17**:208, 1914.

5. Heuer, G. J., and Vail, T. D., Jr.: Chronic Cisternal Arachnoiditis Producing Symptoms of Involvement of the Optic Nerves and Chiasm: Pathology and Results of Operative Treatment in Four Cases, Arch. Opth. **5**: 334 (March) 1931.

TUBEROUS SCLEROSIS DIAGNOSED WITH CEREBRAL PNEUMOGRAPHY

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Tuberous sclerosis is a congenital disease, believed to be comparatively rare, characterized by nodular tumor masses in the convolutions and paraventricular regions of the brain, with clinical manifestations of epilepsy and mental deterioration. Tumors of the skin and heart and of the kidneys and other visceral organs are not infrequently associated with this condition.

Some writers have given von Recklinghausen credit for reporting the first case in 1862.[1] In a brief article, without offering a diagnosis, he reported the results of the necropsy of a new-born infant which showed a number of sclerotic areas in the brain and several myomas projecting into the ventricles of the heart.

The name "tuberous sclerosis" was first introduced by Bourneville in 1880. He was the first to recognize that this condition is a definite entity, and he contributed much of the present knowledge of this disease in a series of articles from 1880 to 1898.[2] He also noted the frequent coexistence of tumors of the kidneys and adenoma sebaceum with this condition but did not think it was possible to diagnose this syndrome during life. His accounts were derived mainly from pathologic studies.

REPORT OF A CASE

History.—M. T. R., a girl aged *2* years and 1 month, was admitted to the University Hospital on Feb. 27, 1931, for an operation for cleft palate and cleft lip. The father, aged 30, left school in the sixth grade at the age of 16. He had several convulsive seizures of unknown etiology when a child but had had none since. He had six brothers and three sisters, only four of whom reached the eighth grade, and these four were all past 16 years of age. One brother and one sister had epileptiform seizures. The father's parents were of low intelligence and had been supported by the county for many years.

The mother, aged 24, left school in the third grade at the age of 10 years, finding school work too difficult to continue. She had three sisters who were apparently of normal intelligence. No definite information was obtained regarding her parents. She was married in 1929 and had four children. Her first child (E. J. R.), a boy, died twelve days after birth because of malnutrition and pneumonia; he had no convulsions. The second (M. T. R.) was the child

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1. von Recklinghausen, F.: Ein Herz von einem Neugeborenen, Monatschr. f. Geburtsh. u. Frauenkr. **20**:1, 1862.

2. Bourneville: Sclérose tubéreuse des circonvolutions cérébrales: idiotie et épilepsie hémiplégique, Arch. de neurol. **1**:81, 1880. Bourneville and Brissaud, E.: Encéphalite ou sclérose tubéreuse des circonvolutions cérébrales, ibid. **1**:397, 1880-1881. Bourneville: Idiotie et épilepsie symptomatique de sclérose tubéreuse ou hypertrophique, ibid. **10**:29, 1900.

whose case is reported here. The third (R. R.) was a girl aged 1 year and 8 months. She was normal physically and neurologically and had not had convulsions. She was definitely retarded mentally, her intelligence quotient on the basis of the Kuhlmann revision of the Stanford-Binet test being 55 per cent. Pneumography by the cisternal route gave negative results. A rather exaggerated notch in the posterior end of the lateral ventricle was present, but this is probably a normal finding, according to Penfield,[3] and should not be mistaken for a nodule of a tumor projecting into the lumen of the ventricle (fig. 1). The fourth child (J. R.), a boy, born in September 1933, died of an undiagnosed condition four months after birth; he had bilateral congenital cleft lip and cleft palate. He had no convulsions. In January 1934 the mother's intelligence quotient was 50 per cent, and she was committed to the custody of the State Board of Control for sterilization because of feeblemindedness. She was admitted to the University Hospital for study in May 1934 and was found to be normal physically and neurologically. There was no history of convulsions, and no cutaneous anomalies were seen. Roentgenograms of the skull and encephalograms were normal.

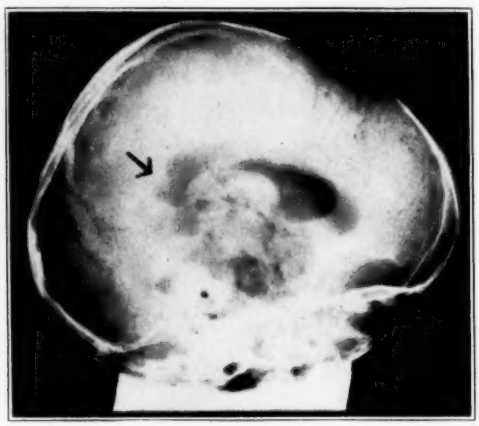

Fig. 1.—Cerebral pneumogram of R. R., sister to M. T. R., taken on April 21, 1934 (partially oblique lateral view). Note the deep notch (marked by arrow) in the superior surface of the posterior horn of the right lateral ventricle. This notch is a normal finding and should not be interpreted as a tumor.

Examination and Course.—When admitted to the hospital the patient (M. T. R.) was undernourished and underdeveloped and had complete bilateral congenital cleft palate and cleft lip; otherwise, she was essentially normal physically and neurologically. The cleft palate was repaired, and the patient was discharged on May 14, 1931. No note was made at that time in regard to her mental status.

Three months later, at the age of 2 years and 5 months, she began to have typical epileptiform seizures. She had about three attacks daily for three or four days and was free from attacks for intervals of from three to seven days. On Oct. 13, 1932, she returned to the University Hospital. She continued to have convulsions with loss of consciousness during her stay in the hospital. A ketogenic diet did not decrease the number of attacks.

3. Penfield, W. G.: Cerebral Pneumography, Arch. Neurol. & Psychiat. **13**: 580 (May) 1925.

During the second admission to the hospital she was observed to be mentally retarded. She was unable to sit up without assistance and could not talk. A spinal puncture was performed, and the fluid found to be under normal pressure.

Encephalography was performed, 50 cc. of spinal fluid being replaced by 40 cc. of air. The roentgen findings (figs. 2 and 3) at that time were: No air could be

Fig. 2.—Cerebral pneumogram of M. T. R. taken on Nov. 1, 1932 (right lateral prone position). The lateral, third and fourth ventricles are well visualized. The lateral ventricles show moderate dilatation, especially of the anterior horn. Four rounded, sharply defined tumor-like dense areas (arrows) can be visualized projecting into the lumen of the lateral ventricles.

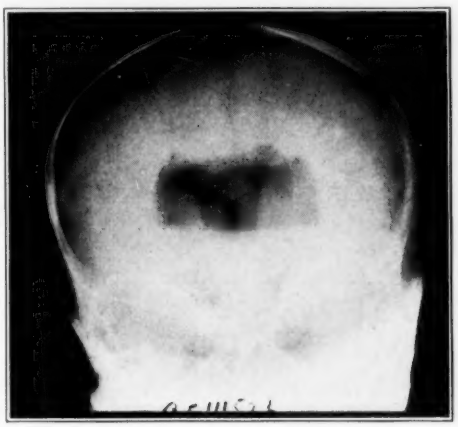

Fig. 3.—Cerebral pneumogram of M. T. R. taken on Nov. 1, 1932 (antero-posterior upright position). The nodules are shown projecting from the superior surface of both lateral ventricles. A fluid level is apparent. The shadow of the septum pellucidum is absent, the two lateral ventricles appearing to be continuous.

visualized in the subarachnoid spaces. The ventricles were all well filled with air and showed a normal form with moderate general enlargement. The septum pellucidum was apparently absent. There was a bizarre deformity of the lateral ventricles with at least four rounded, sharply defined masses projecting into the lumen. These appeared to arise from the superior, lateral, inferior and posterior

surfaces of the ventricles. Their appearance suggested multiple tumors in close relationship to the ventricles. The skull itself showed some evidences of hydrocephalus, the anterior fontanel and the sutures being much more open than is normal for this age. There was no evidence of other pathologic changes in the bones of the skull.

Fig. 4.—Photograph of M. T. R., showing a lack of expression, large distance between the eyes and defect from cleft lip.

Fig. 5.—Cerebral pneumogram of M. T. R. taken on Feb. 27, 1934 (right lateral prone position). The findings are similar to those shown in figure 2 except that the nodules are more easily defined. The growth in size of the ventricles is in proportion to the growth of the skull, but the nodules do not appear to have increased in size.

Laboratory Tests: Serologic tests of the blood and spinal fluid gave negative results.

Subsequent Course.—Feb. 8, 1934, the patient returned to the hospital on request for further study. It was learned that she had had no convulsive seizures following the injection of air for encephalography (November 1932), although she had received no treatment. Physical examination revealed that the patient was still undernourished and underdeveloped. The space between the eyes was greater than is seen in normal children, and a scar from the repair of the cleft lip was present (fig. 4). No cutaneous anomalies were noted. Neurologic examination gave essentially normal results. Mentally the patient appeared to be definitely subnormal. She had no voluntary control of the sphincters. Her gait was very unsteady and she was able to say only "mama" and "papa." With the Kuhlmann revision of the Stanford-Binet intelligence test the intelligence quotient was 52 per cent.

A second encephalogram (fig. 5) was made on Feb. 24, 1934, by the spinal route, 60 cc. of spinal fluid being replaced with 50 cc. of air. The spinal fluid pressure was again found to be normal (110 cm. of water). There was a considerable accumulation of air in the subarachnoid spaces in both parietal regions. There was also a rather large quantity in the subdural space of the right superior parietal region. All the ventricles were well filled with air. Aside from the normal increase in size no pronounced change in the appearance of the ventricles since the last examination in November 1932 could be observed. The continuity of the two lateral ventricles remained the same. The nodules of the tumor appeared to be of about the same size and in the same position.

Examination of the skull showed a slight thinning of the inner table and a rather scaphoid shape, suggesting slight hydrocephalus. There was no other evidence of abnormality. Roentgenograms of the wrists, hands, knees and spine showed them to be normal in osseous development. Intravenous urography revealed no evidence of abnormality of the renal pelves, and the kidneys themselves appeared normal. Roentgenograms of the heart and lungs revealed no abnormalities.

COMMENT

This case is of particular interest because of the unusual roentgenographic picture of the ventricles of the brain obtained by injection of air. The appearance of the shadows projecting into the lumen of the ventricles is unique and may represent a pathognomonic sign of tuberous sclerosis. These subependymal tumor masses, clearly visualized in the cerebral pneumographs, are commonly seen in the gross examination of the brain in cases of tuberous sclerosis. We have found only two cases in which encephalograms or ventriculograms have been reported in suspected cases of tuberous sclerosis. Yakovlev and Guthrie [4] reported a case of neurofibromatosis with epilepsy from early infancy, which they believed is closely associated with tuberous sclerosis. An encephalogram showed "the lateral ventricles dilated, and there are irregular masses behind the thalamus resembling 'candle gutterings' and suggesting tumors of the choroid plexus in the region of the pineal gland." The illustration was not particularly clear nor was it as convincing as the pneumograms in the case reported in this article. Stewart and Bauer [5] reported a case of tuberous sclerosis with cerebral pneumograms showing

4. Yakovlev, P. I., and Guthrie, R. H.: Congenital Ectodermoses (Neurocutaneous Syndromes) in Epileptic Patients, Arch. Neurol. & Psychiat. **26**:1145 (Dec.) 1931.

5. Stewart, H. L., and Bauer, E. L.: Tuberous Sclerosis, Arch. Path. **14**:799 (Dec.) 1932.

dilated ventricles but no tumor masses. They, however, were unable to demonstrate any tumors projecting into the ventricles at autopsy.

Ventriculograms made in cases of other conditions may resemble those seen in cases of tuberous sclerosis, but the history and clinical findings should at once help in differential diagnosis. Learmonth and Camp [6] reported a case of multiple tumor implants in the ventricles arising from a medulloblastoma of the fourth ventricle revealed by ventriculography. Such tumor implants may resemble the subependymal tumors present in tuberous sclerosis. The apparent absence of the septum pellucidum is difficult to explain. Hydrocephalus does not appear to be of sufficient degree to cause such a complete disappearance of the shadow of the septum. It would appear that this is probably an accompanying congenital anomaly of a rather unusual type.

Delay in mental development is usually the first clinical symptom of tuberous sclerosis. Epileptiform seizures usually appear within the first two years of life and are similar to those in idiopathic epilepsy. The differentiating characteristic of these seizures is the long remissions which occur between series of attacks, irrespective of treatment. Adenoma sebaceum, a cutaneous abnormality, occurs only occasionally at birth, frequently during childhood and almost invariably before or during puberty.

Many cases are incomplete or abortive, and one or more of the three cardinal symptoms may be absent (Schuster [7] and Critchley and Earl [8]). Stigmas of degeneration are frequently seen in persons with this condition. A high, narrow palate, a cleft palate, spina bifida and other congenital anomalies are fairly common.

The lesions in the brain appear grossly as hard white or gray nodules which are more readily recognized by touch than by sight. They vary in number from one or two to twenty or thirty and in size from 0.5 to 4 cm. in diameter, and they are found in the cerebral convolutions and beneath the ependyma, projecting into the ventricles like grapes. The microscopic picture of this condition has been excellently described by Globus.[9]

CONCLUSIONS

1. Tuberous sclerosis may be a more common disease than has been generally believed. It should be considered in the differential diagnosis in every case of dementia associated with epilepsy.

2. Since abortive and monosymptomatic forms exist, cerebral pneumography may prove invaluable in establishing a diagnosis. The roentgen findings appear to be characteristic of the condition.

3. Cerebral pneumography after an interval of sixteen months showed practically no change, indicating that the condition may run a very insidious course.

Dr. Irvine McQuarrie, chief of the department of pediatrics, permitted us to report this case.

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6. Learmonth, J. R., and Camp, J. D.: Multiple Tumor Implants in the Ventricles Revealed by Ventriculography, Am. J. Roentgenol. **29**:393, 1933.

7. Schuster, P.: Beiträge zur Klinik der tuberösen Sklerose des Gehirns, Deutsche Ztschr. f. Nervenh. **50**:96, 1913.

8. Critchley, Macdonald, and Earl, C. J. C.: Tuberose Sclerosis and Allied Conditions, Brain **55**:311, 1932.

9. Globus, J. H.: Tuberose Sclerosis, in Penfield, Wilder: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, p. 1150.

INTRACRANIAL CHORDOMA

Report of a Case

LEONARD T. FURLOW, M.D., ST. LOUIS

The first description of the spheno-occipital remnant of the notochord was made by Virchow,[1] but he considered this jelly-like tissue to be degenerated cartilage. In describing a tumor arising from it he failed to see the relation between the tumor and the notochordal tissue. Although Muller[2] had pointed out this relation in 1858, the erroneous teaching of Virchow was not corrected until the work of Ribbert[3] in 1894. These authors showed conclusively that although the tissue always lies next to cartilage, it is independent of the cartilage.

In 1864 Klebs[4] reported the case of a patient who died in convulsions. A tumor of this type was found at autopsy. Since that time an increasing number of cases have been reported. However, the tumor is uncommon enough to warrant the report of individual cases, particularly if the diagnosis is made at biopsy. For a review of the literature and a complete study of the tumors, the works of Jelliffe and Larkin,[5] Stewart and Morin[6] and others[7] may be referred to.

From the Department of Neurological Surgery, Washington University School of Medicine, and the Barnes Hospital.

1. Virchow, R.: Untersuchungen über die Entwickelung des Schädelgrundes, Berlin, Georg Reimer, 1857.

2. Muller, H.: Ueber das Vorkommen von Resten der Chorda dorsalis bei Menschen nach der Geburt und über ihr Verhältnis zu den Gallertgeschwülsten am Clivus, Ztschr. f. rat. Med. **2**:202, 1858.

3. Ribbert, H.: Ueber die Ecchondrosis physalifora spheno-occipitalis, nach Untersuchungen von Hermann Steiner, Centralbl. f. allg. Path. u. path. Anat. **5**:457, 1894.

4. Klebs, E.: Ein Fall von Ecchondrosis spheno-occipitalis amylacea, Virchows Arch. f. path. Anat. **31**:396, 1864.

5. Jelliffe, S. E., and Larkin, J. H.: Malignant Chordoma Involving Brain and Spinal Cord, J. Nerv. & Ment. Dis. **39**:1, 1912.

6. Stewart, M. J., and Morin, J. E.: Chordoma: A Review, with Report of a New Sacrococcygeal Case, J. Path. & Bact. **29**:41, 1926.

7. (*a*) Daland, E. M.: Chordoma, Boston M. & S. J. **180**:571, 1919. (*b*) Burrow, J. le F., and Stewart, M. J.: Malignant Spheno-Occipital Chordoma, J. Neurol. & Psychopath. **4**:205, 1923. (*c*) Eckel, J. L., and Jacobs, W. F.: Malignant Spheno-Occipital Chordoma, J. Nerv. & Ment. Dis. **61**:471, 1925. (*d*) Hass, G. M.: Chordomas of the Cranium and Cervical Portion of the Spine, Arch. Neurol. & Psychiat. **32**:300 (Aug.) 1934. (*e*) Bailey, Percival, and Bagdasar, Dumitri: Intracranial Chordoblastoma, Am. J. Path. **5**:439, 1929. (*f*) Van Wagenen, W. P.: Personal communication to Dr. Sachs. Chordoblastoma of the Basilar Plate of the Skull and Ecchordosis Physaliphora Spheno-Occipitalis: Suggestions for Diagnosis and Surgical Treatment, Arch. Neurol. & Psychiat. **34**:548 (Sept.) 1935.

REPORT OF CASE

History.—M. A. M., a white woman aged 60, married, was referred by Dr. E. G. Gill, of Roanoke, Va., to the neurosurgical service of Dr. Ernest Sachs on Oct. 19, 1934, with a complaint of total blindness and of nasal obstruction. The family history was unimportant. The general health of the patient had always been excellent. The menopause occurred when she was 48. Menstruation had been regular and normal prior to this time.

From four to five years before admission, during the course of a general examination, she learned that she had high blood pressure. The systolic blood pressure varied between 180 and 200 most of the time. Except for this hypertension, the patient considered herself perfectly well until about twenty-two months

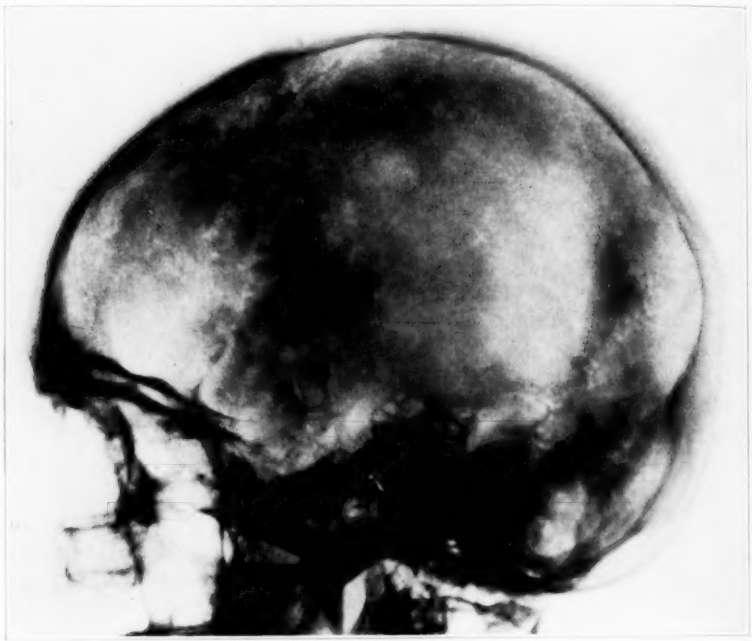

Fig. 1.—Roentgenogram showing marked destruction of the region of the sella with scattered areas of calcification throughout this region.

before admission, when she noticed that vision in the right eye was failing rather rapidly. Within a period of from six to seven months the eye became totally blind and about fifteen months before admission failing vision in the left eye was noticed. The left eye also became blind, so that about eight months before admission to the hospital the patient had lost the sight of both eyes. Light perception was not retained. About fifteen months before admission the patient began to have difficulty in breathing through her nose. This condition progressed steadily, and for several months she had been unable to breathe through the nose and there had been some change in the quality of the voice. For six months there had been a gradual diminution in the acuity of hearing, more pronounced in the left ear than in the right. She was still able to hear the spoken voice but with

considerable difficulty. There had been no headaches and no loss of weight throughout the course of the illness.

Examination.—General physical examination showed total blindness, complete bilateral nasal obstruction and a blood pressure of 200 systolic and 110 diastolic. There was definite arteriosclerosis.

Neurologic examination showed normal mental reactions and responses. The head was normal in size and shape. There was bilateral loss of the sense of smell. Ophthalmoscopic examination showed bilateral primary atrophy of the optic nerve with complete loss of vision and loss of pupillary reaction. Both corneal reflexes were absent. There was diminished hearing in both ears, more pronounced in the left than in the right. Aerial conduction was better than bone conduction on both sides. The gag reflex was markedly diminished, and when

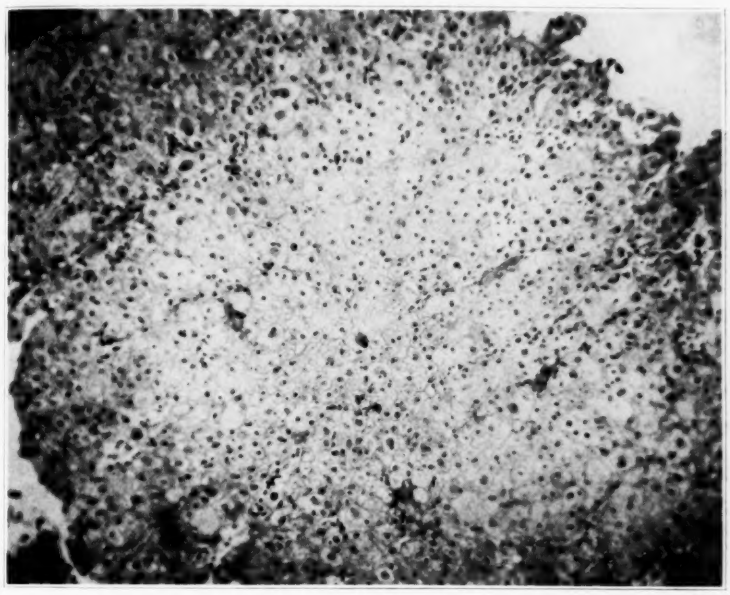

Fig. 2.—Photomicrograph (low power) of the tumor, showing arrangement of the blood vessels to the tumor cells. Magnification, × 100.

the soft palate was retracted upward a large, smooth, rounded mass was seen in the nasopharynx. The surface of the portion of the tumor presenting itself in the nasopharynx was relatively avascular. The results of neurologic examination otherwise were entirely negative.

Laboratory examinations showed nothing of importance. The basal metabolic rate was —4.

Roentgen ray examination of the skull (fig. 1), with the right side toward the film, showed that the sella, including the floor and dorsum, had been destroyed completely and that there was some erosion of the anterior clinoid process. Scattered throughout this area were numerous patches of calcification. Attempts to take roentgenograms of the optic foramina were unsuccessful because these passages were obscured by overlying calcification.

Course.—On Oct. 20, 1934, the patient was seen by Dr. M. F. Arbuckle, who noted: "This patient has a huge tumor in the nasopharynx. Its surface is smooth, and there is no sign of ulceration. It fills the vault completely. The same mass continues forward into the right side of the nose about half-way to the vestibule. It is visible on the left side also but does not extend as far forward. The appearance is that of a benign rather than that of a malignant tumor."

On Oct. 22, 1934, a biopsy of the mass in the nasopharynx was considered. When the soft palate was retracted and the mass examined more thoroughly, it seemed to pulsate, and its surface so closely resembled dura that it was decided that it would not be advisable to incise it. A small piece of tissue for biopsy was taken from the mass in the nasal cavity. From this tissue a diagnosis of chordoma

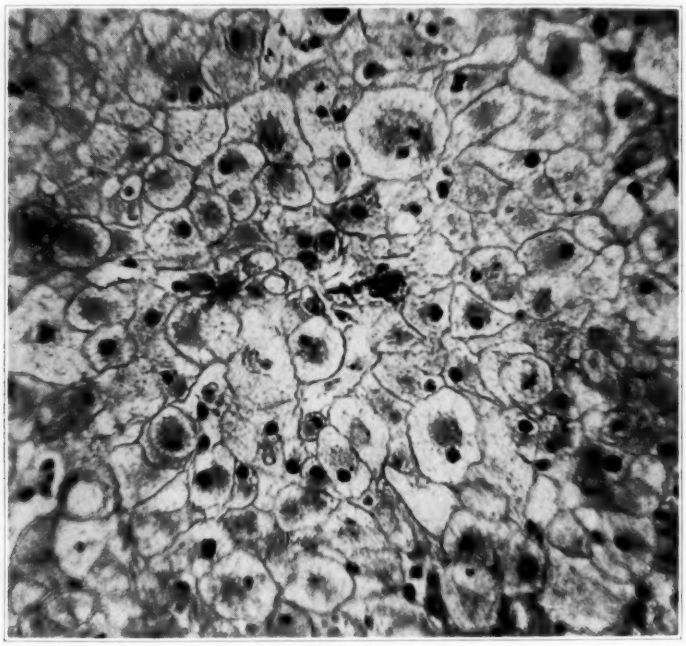

Fig. 3.—Photomicrograph (high power) of the section shown in figure 2. The cells resemble those seen in the embryonic notochord. The marked vacuolation is apparent as well as the clearly defined cell membrane. Magnification, × 430.

was made. High voltage roentgen therapy was given as a palliative procedure, and the patient was discharged on Oct. 26, 1934.

Report of Biopsy.—The amount of tissue removed was small. It was fixed in Zenker's fluid. Tissue was available only for the hematoxylin and eosin and the Mallory phosphotungstic acid stain (figs. 2 and 3). The tissue was composed of large, irregularly shaped cells with sharply outlined cell membranes, which stained deeply with Mallory's phosphotungstic acid hematoxylin. The nuclei were small, deeply stained and eccentrically located. The cytoplasm was granular and showed considerable vacuolation, which tended to occur in the periphery of the cells, giving the impression of a central condensation of cytoplasmic substance.

No mitoses were seen. There was a faint reticulum, but supporting structures were, for the most part, absent. No necrosis was observed, although vascularization was not marked.

COMMENT

Because of the age of the patient, the extent and size of the tumor shown by roentgenograms and examination of the nose and throat and the fact that blindness was complete, surgical intervention was considered unwise. Bailey and Bagdasar [7e] reported one case with operation by Cushing and recovery, but the patient was not totally blind and the tumor was much smaller. Van Wagenen [7f] also reported a case of operation with partial removal through the posterior fossa, but at the time of his report the tumor had recurred.

In the case reported by Daland [7a] massive doses of roentgen rays were given after operation with some apparent retardation of growth. However, in this instance the tumor presented itself in the neck, and there was a local recurrence after seven months. On the basis of this meager evidence, high voltage roentgen therapy has been given by Dr. Sherwood Moore, but after three months of irradiation there has been no improvement in the condition of the patient.

EPENDYMOBLASTOMA IN THE FOURTH VENTRICLE, WITH NEW BONE FORMATION

ROLAND P. MACKAY, M.D., CHICAGO

The presence of newly formed bone in the cranial cavity is apparently rare except in the meninges and falx, where deposition of calcium and ossification frequently have been reported.[1] The formation of bone within the brain itself is extremely uncommon. In the older literature a few reports of "osteoma" of the brain may be found,[2] but recently there has been a tendency to abandon the term osteoma because of the difficulty of deciding when bone is neoplastic.[3] From

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From the Department of Neurology, St. Luke's Hospital, Chicago.

1. Cleland, J.: Description of Two Tumors Adherent to the Deep Surface of the Dura Mater, Glasgow M. J. **11**:148, 1864. Potts, William: Osseous Deposit in the Arachnoid, Tr. Path. Soc. London **25**:3, 1874. Burton, F. H. M.: Case of Osteophytes of the Arachnoid, Lancet **1**:1084, 1887. Cushing, H., and Weed, Lewis H.: Studies on the Cerebrospinal Fluid and Its Pathway: IX. Calcareous and Osseous Deposits in the Arachnoidea, Bull. Johns Hopkins Hosp. **26**:367, 1915. Halstead, A. E., and Christopher, F.: Calcification and Ossification of the Meninges, Arch. Surg. **6**:847 (May) 1923. Weiser, Arthur: Zur Kenntnis der Knochenbildung an der zerebralen Fläche der Duraendotheliome, Deutsche Ztschr. f. Chir. **192**:405, 1925. Bailey, P., and Bucy, P. C.: The Origin and Nature of the Meningeal Tumors, Am. J. Cancer **15**:15, 1931.

2. Bristowe: Tumor Connected with the Brain, Consisting of True Bone, Tr. Path. Soc. London **6**:25, 1854. Benjamin, Ludwig: Beschreibung einer Knochengeschewulst im Gehirn, Virchows Arch. f. path. Anat. **14**:552, 1858. Ranvier: Tumeur osseuse du cervelet, Bull. Soc. anat. de Paris **7**:219, 1862. Virchow, Rudolf: Hirn-Osteome, in Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1864, vol. 2, p. 96. Meschede, Franz: Osteom des grossen Gehirns und Ventrikelbildung in Ammonshorn, beobachtet bei einem Epileptischen, Virchows Arch. f. path. Anat. **35**:472, 1866. Ebstein, Wilhelm: Grosses Osteom der linken Kleinhirnhemisphäre, Virchows Arch. f. path. Anat. **45**:145, 1870. Bidder, A.: Ein Osteom des Corpus striatum bei Hemiplegia infantilis, Virchows Arch. f. path. Anat. **88**:91, 1882. Witkowski, L.: Ueber Knochen- und Concrementbildung im Gehirn, Arch. f. Psychiat. **14**:415, 1883. Love, John: Two Cases of Osteoma of the Brain, Tr. Glasgow Path. & Clin. Soc. **2**:47, 1884-1886. Fraser, Donald: Specimen of Osseous Tumour of the Brain, Glasgow M. J. **42**:380, 1894. Walker, J. W.: A Case of Primary Osteoma of the Brain, Rep. Soc. Study Dis. Child., London **2**:173, 1901-1902.

3. (*a*) von Lehoczky, T.: Ueber die Knochenbildungen des Gehirns, Virchows Arch. f. path. Anat. **265**:366, 1927. (*b*) Berner, O.: Berichte über zwei knochenthaltende intracerebrale Knoten und eine knochenhaltige Gehirngeschwulst von meningealer Herkunft, Virchows Arch. f. path. Anat. **270**:487, 1928.

a study of the available reports, formation of new bone would seem to occur within the brain substance under three sets of conditions:

1. Calcification and ossification of intracerebral hemorrhages and scars apparently may occur rarely. Brunner,[4] Leriche and Policard[5] and Berner[3b] have reported cases of this kind. There is, however, always some doubt whether the meninges participate in the formation of bone, especially in those cases in which trauma has been a factor.

2. Intracranial ossification apparently may occur around certain parasitic cysts, such as Cysticercus,[3b] Coccidium oviforme[6] and perhaps Echinococcus. Berner stated that tuberculomas of the brain may become the seat of ossification, and presumably gummas may be subject to similar change. In most of these reports there is doubt about the exact nature of the lesion which gives rise to bone, but the participation of the meninges scarcely ever can be ruled out.

3. Undoubtedly the most common type of intracerebral formation of bone occurs in the mixed tumors or teratomas. These tumors are found most often in the pineal region or about the tuber cinereum, where embryologic malformations readily occur. Hosoi[7] has recently made a study of teratomas of the brain. Many other reports of tumors of this type containing bone may be found in the literature.[8] The older reports of osteoma of the brain probably are best classified in this group, even those in which only bone seemed to be present, since one tissue in a teratoma may overwhelm the others.

No matter under what conditions it occurs, the formation of bone seems to depend on the presence of mesoblastic tissue. Aside from the meninges, the only mesoblastic tissue in the brain is in the walls of the blood vessels, and apparently it produces bone on rare occasions or under exceptional circumstances. It is possible that the bone which is said to be formed in cerebral hemorrhages and scars and about parasitic cysts is produced by mesoblastic cells in the walls of the blood vessels, but there is no direct evidence of this. It can be stated that, with rare and debatable exceptions, intracranial new bone is formed only by the meninges or in the mixed or teratomatous growths.

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4. Brunner, Hans: Ueber Verkalkung und Knochenbildung in Hirnnarben, Ztschr. f. d. ges. Neurol. u. Psychiat. **72**:193, 1921.

5. Leriche, R., and Policard, A.: De la formation intracérébrale d'os nouveau au contact d'esquilles mortes incluses, Bull. et mém. Soc. d. chirurgiens de Paris **45**:580, 1919.

6. Thomas, John Jenks: Bone Tumor in the Human Brain Surrounding Encysted Coccidia Oviformia, M. & S. Rep. Boston City Hosp. **10**:102, 1899.

7. Hosoi, Kiyoshi: Teratoma and Teratoid Tumors of the Brain, Arch. Path. **9**:1207 (June) 1930.

8. Maier, Rudolf: Combinierte Geschwulst im Grosshirn, Virchows Arch. f. path. Anat. **20**:536, 1861. Strassmann, Fritz, and Strecker, Carl: Ein Teratom im rechten Seitenventrikel, Virchows Arch. f. path. Anat. **108**:351, 1887. Saxer, F.: Ein zum grössten Theil aus Derivaten der Medullarplatte bestehendes grosses Teratom im III Ventrikel eines sieben wöchentlichen Kindes, Beitr. z. path. Anat. u. z. allg. Path. **20**:399, 1896. Kon, Jutaka: Hypophysenstudien. I. Seltene Tumoren der Hypophysengegend (Teratom, Peritheliom, telangiektatisches Sarkom), Beitr. z. path. Anat. u. z. allg. Path. **44**:233, 1908. Derman, G. L.: Zur Kenntnis der Teratome des Gehirns, Virchows Arch. f. path. Anat. **259**:767, 1926. Jakob, Christofredo, and Pedace, Eduardo A.: Fibro-condro-osteoma primitivo del cerebro, Rev. Asoc. méd. argent. **47**:2435 (April) 1933. Schuster, Helene: Ein das Hirn ersetzendes Teratom in der Schädelhöhle eines Neugeborenen, Centralbl. f. allg. Path. u. path. Anat. **59**:163 (Dec. 30) 1933.

The tumor which is the subject of this report is a growth of mixed origin. It is interesting, furthermore, as an illustration of the close relationship existing between embryologic malformations and neoplasms.

REPORT OF A CASE

Intermittent vomiting for one year in a boy aged 4½ years, with later appearance of headaches. Clinical picture of internal hydrocephalus and cerebellar dysfunction. Operation. Ependymoblastoma in the fourth ventricle, with formation of new bone.

History.—R. C., a boy aged 4½ years, whose past and family history is without significance, was referred by Dr. Henry W. Cheney, of Chicago, to the service of Dr. George W. Hall at St. Luke's Hospital on Dec. 7, 1933. Since January 1933 he had suffered every month or so from attacks of vomiting, between which he had been apparently normal. Six weeks prior to admission to the hospital, he began to have a constant dull headache and an unsteady gait. Vomiting began again a week before entrance, and at that time a spinal puncture revealed a normal fluid under greatly increased pressure. On the day before admission he had a generalized convulsion.

Examination.—The boy was drowsy and had an ataxic gait. A moderate degree of papilledema was present on both sides. The pupils were equal in size and somewhat dilated, and they responded sluggishly to light. There was gross horizontal nystagmus to the right; there was no palsy of the cranial nerves and no weakness of the musculature of the body. The biceps, triceps and patellar reflexes were hyperactive; the abdominal reflexes were not obtained. There were positive Babinski responses and moderate talipes equinus bilaterally. The urine was normal. The erythrocytes numbered 3,780,000 and the leukocytes 13,200 per cubic millimeter. There was 15.12 Gm. of hemoglobin per hundred cubic centimeters of blood (74 per cent). Roentgenograms of the skull revealed increased convolutional markings, widening of the sutures, a relatively normal sella turcica and a radiopaque mass in the posterior fossa.

Operation.—Dr. Eric Oldberg made a cerebellar exploration on December 8 and found "a large, reddish-gray, firm tumor in the fourth ventricle, bulging down into the foramen magnum." Approximately five sixths of the tumor was removed, including a very hard, apparently calcified and superficially knobby mass which lay in the fourth ventricle. Manipulation of the base of the tumor, which seemed to infiltrate the underlying medulla, stopped the patient's respiration which had to be restored by artificial means. Consequently this part of the tumor was left in place.

Course.—After the operation the patient's general condition was poor, and he died of respiratory failure at midnight of the same day.

Pathologico-Anatomic Examination.—Macroscopic Observations: The portion of the tumor removed at operation consisted of soft, grayish-white tissue, totaling about 4 ounces (118 cc.) in volume, and the aforementioned hard, nodular mass, which measured 2.2 by 2 by 1.7 cm. (fig. 1). The outer surface consisted of an irregular, pearly-white, hyaline, fibrous layer, while the interior, which was exposed on breaking the mass, was composed of fairly compact bone.

Postmortem examination revealed marked hydrocephalus but no other abnormality of the cerebrum. The fourth ventricle was represented by a large cavity from which most of the tumor had been removed. The growth had extended far enough into the cerebellar hemispheres to involve portions of the dentate nuclei.

The floor of the cavity was formed by the dorsal surface of the medulla, to which tags of tumor tissue were attached. Some hemorrhage had involved the medulla and the cerebellum beyond the limits of the cavity. Examination of the remainder of the body revealed nothing abnormal. Unfortunately the spinal cord was not examined.

Microscopic Observations: All the tissues for examination were fixed in solution of formaldehyde. Portions of the tumor removed at operation were mounted in paraffin and stained with hematoxylin and eosin and with Mallory's phosphotungstic acid-hematoxylin method, while other pieces were cut with a freezing microtome and stained by the gold sublimate method of Cajal and by Bielschowsky's axis-cylinder stain. The hard nodule removed at operation was decalcified, sectioned and stained by Mallory's phosphotungstic acid-hematoxylin method. Sections from the cerebellum were mounted in paraffin and stained with hematoxylin and eosin and with phosphotungstic acid and hematoxylin, while other portions of the cerebellum and medulla were mounted in pyroxylin (celloidin) and stained by Van Gieson's method, Mallory's aniline blue method, Davenport's silver impregnation method and Weil's method for myelin sheaths.

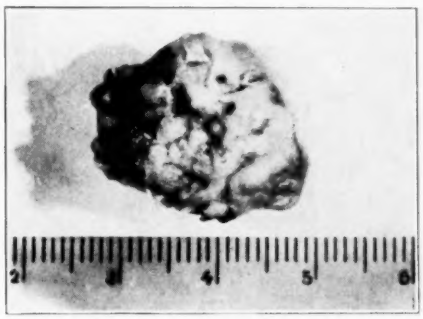

Fig. 1.—Gross specimen of bone removed at operation.

The tumor tissues were largely a conglomerate mixture of ependymal and glial cells in various stages of development. In several areas the cuboidal ependymal cells, with their eosinophile cytoplasm, ovoid nuclei and fine granules of chromatin, formed tubules (fig. 2). These cells often contained blepharoplasts next the lumen. At times these cells ranged themselves in a columnar layer around slit-shaped cavities and gave rise to fibril-forming processes from their outer ends. In other areas similar cells were laid down in sheets, their eosin-stained cytoplasm possessing indistinct borders. Scattered between these cells were spongioblasts with one or two poles bearing heavy, tortuous fibrils. The nuclei of the spongioblasts were rich in chromatin, stained deeply with phosphotungstic acid and hematoxylin and contrasted strikingly with the vesicular nuclei of the ependymal cells (fig. 3). In still other areas the spongioblasts outnumbered all other cells and often were arranged in perivascular palisades (fig. 4).

In many parts of the tumor there was a tissue which was made up of a closely woven net of glia fibrils, in the meshes of which relatively few cells were found. Some of these cells were mature fibrillar astrocytes, while others were ependymal spongioblasts bearing heavy fibrils. This tissue was identical with the primary ependymal gliosis of syringomyelia (fig. 5).

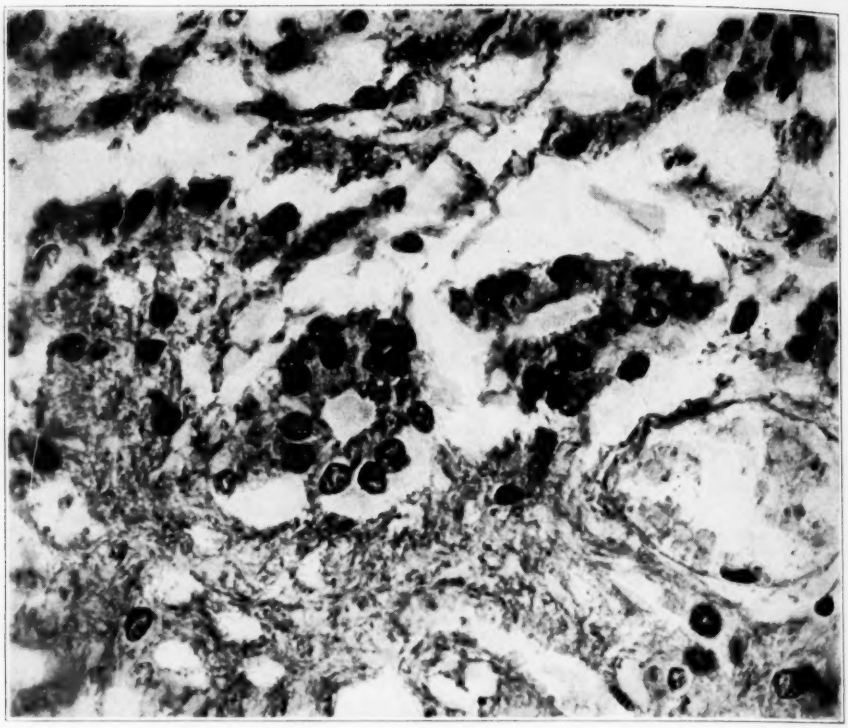

Fig. 2.—Ependymal cells in tubule formation. Blepharoplasts are seen in the cytoplasm next the lumen. Phosphotungstic acid-hematoxylin stain; × 675.

Fig. 3.—Mixture of mature ependymal cells and fibril-forming ependymal spongioblasts. Phosphotungstic acid-hematoxylin stain; × 675.

The vascular supply of the tumor was rather sparse, and the walls of some of the blood vessels were slightly thickened. There was considerable evidence of hemorrhage, mostly recent, not only in the tumor but in the surrounding white matter of the cerebellum and under the ependymal covering of the floor of the fourth ventricle. The ependymal layer was normal in the posterior part of the floor of the fourth ventricle, but in the anterior part it was replaced by tags of tumor tissue remaining from the operation. It was not possible, however, to trace the transition from the normal ependyma to the tumor in the available sections.

Degeneration was in process in a few areas of the tumor. In these regions large mononuclear cells were found, chiefly clustered about blood vessels. The

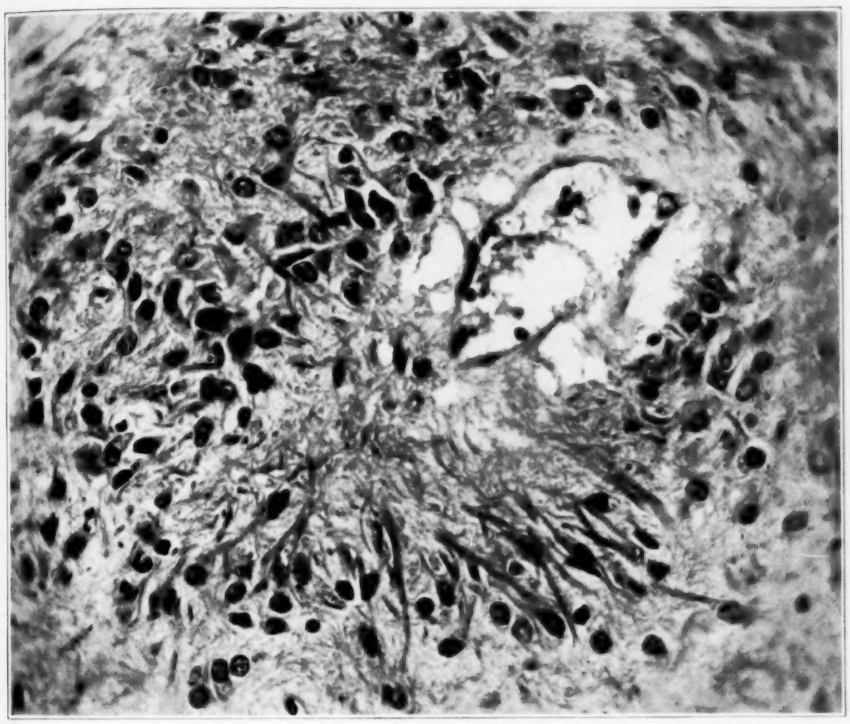

Fig. 4.—Ependymal spongioblasts in palisade formation. Phosphotungstic acid-hematoxylin stain; × 460.

nuclei of these cells were intact and resembled the vesicular nuclei of the ependymal cells of the tumor; the cytoplasm contained numerous small globules, which stained dark blue with phosphotungstic acid and hematoxylin but took no stain with hematoxylin and eosin. These globules were not fat, since they were present in material embedded in paraffin, but they probably represented products of cellular degeneration (fig. 6).

The hard nodular mass removed at operation proved to be cancellous bone. The trabeculae contained lacunae with canaliculi; the intertrabecular spaces were filled with loosely arranged fusiform osteoblasts. The bulk of this bone exhibited active intramembranous ossification, but fibrous cartilage was present at the edges of the mass, where intracartilaginous ossification was in progress. Both the mem-

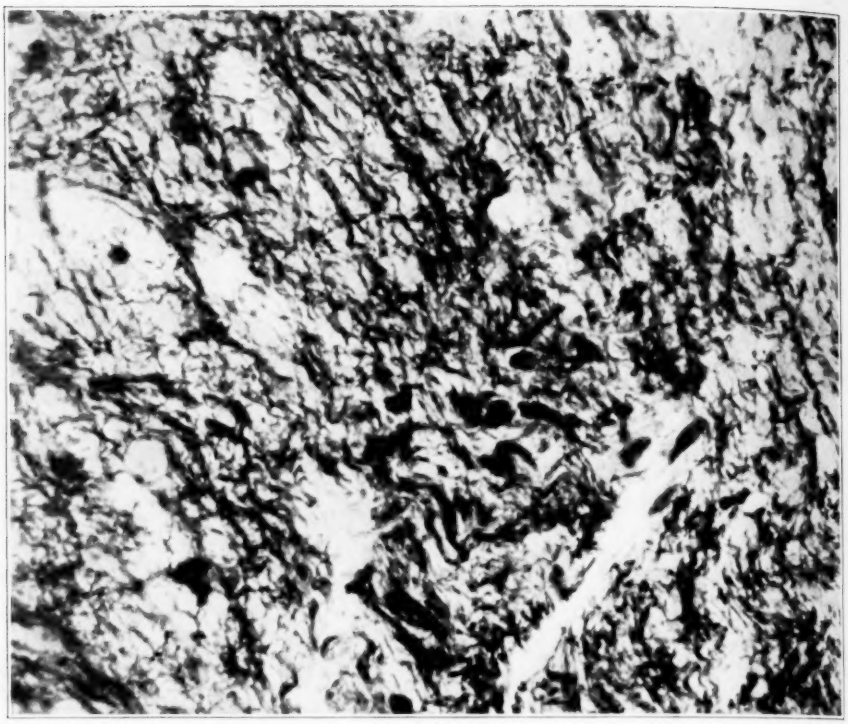

Fig. 5.—Heavy network of glial fibrils, arising from astrocytes and spongioblasts of ependymal origin. Phosphotungstic acid-hematoxylin stain; × 675.

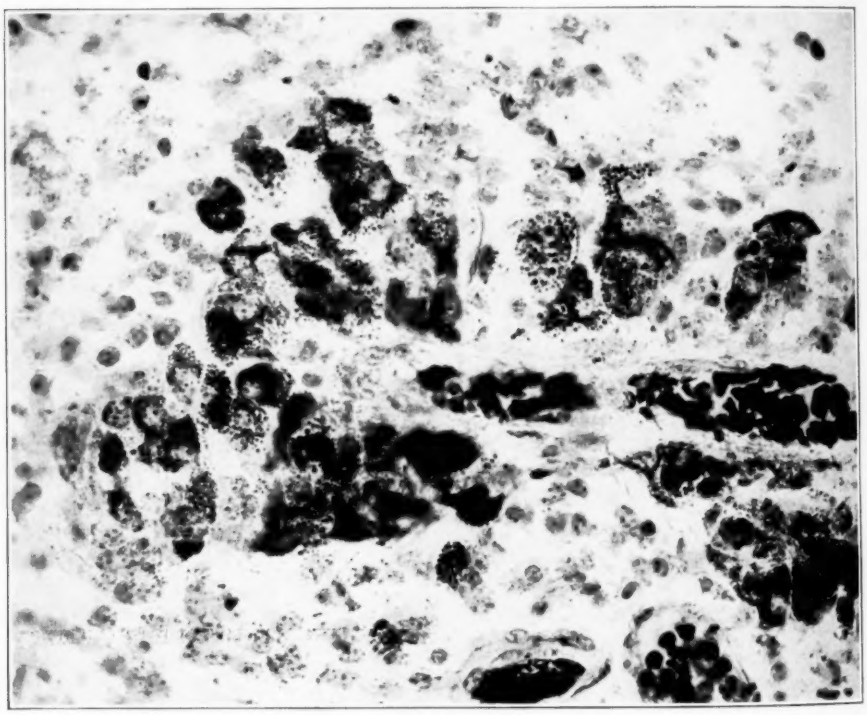

Fig. 6.—Large mononuclear (tumor?) cells in perivascular arrangement containing products of granular degeneration, seen in areas of the tumor undergoing degeneration. Phosphotungstic acid-hematoxylin stain; × 420.

branous and the cartilaginous ossification are illustrated in figure 7. A few other particles of bone were present in the portions of the tumor removed at operation, apart from the main bony mass. Considerable amounts of collagenous connective tissue were found around these smaller fragments of bone, where membranous ossification was in progress too.

COMMENT

It is obvious that in this case the tumor was of mixed ectodermal (ependymal) and mesodermal (bone-forming) origin. Within the ectodermal, or ependymal, portion of the tumor one could identify three outstanding types of cells: (1) rela-

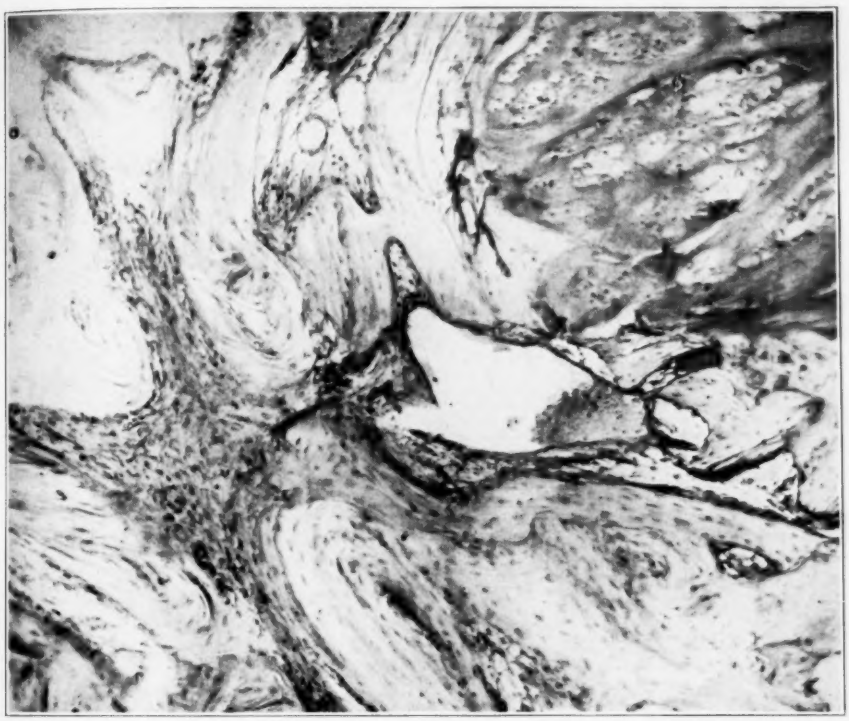

Fig. 7.—Osteoblastoma. Bone trabeculae, with cartilage shown at the upper right corner, where cartilaginous ossification is in progress. At the left, intramembranous ossification is seen. Hematoxylin and eosin stain; × 85.

tively mature ependymal cells, arranged in broad sheets or tubules and often exhibiting blepharoplasts and fibrils (figs. 2 and 3); (2) relatively mature fibrillar astrocytes forming a wealth of fibrils, woven together into a very dense network (fig. 5); (3) ependymal spongioblasts, intermediate between, or ancestral to, the preceding two types, seen profusely mixed both with the ependymal cells (fig. 3) and with the astrocytes (fig. 5) and often numerous (fig. 4).

The rather marked morphologic variations in the tumor depend in part on the proportions in which these types of cells are combined. When the spongioblasts are associated with their adult ependymal descendants, the picture is that

of an ependymoblastoma (fig. 4), which has been well described by Bailey.[9] On the other hand, when they are associated with their other descendants, the mature fibrillar astrocytes, the picture (fig. 5) is that of the primary ependymal gliosis of syringomyelia, recently described in detail by Mackay and Favill.[10] It is definitely demonstrable that these gliomatous areas of the tumor do not represent a reactive, or secondary, gliosis, since they are rich in fibril-forming ependymal spongioblasts as well as in fibrillar astrocytes, as may be seen in figure 5.

Thus portions of the ependymal tumor resemble the ependymomas; others, the ependymoblastomas, and still others, the primary ependymal gliosis of syringomyelia. The best name for the tumor is probably ependymoblastoma, but it really is not described properly in the term. It is evident, however, that the ectodermal portion of this mixed tumor arises from the ependymal cells of the fourth ventricle or from their embryonal antecedents, the germinal cells of the medullary tube. Mackay and Favill,[10] in a recent contribution, pointed out that inadequate and improper closure of the medullary groove (dysraphia) may produce such a disturbance of the germinal cells of the ependymal layer that they will proliferate and form (*a*) primary ependymal gliosis (syringomyelia), or (*b*) various glial tumors, especially ependymoblastoma. Both conditions were present in the case they reported. They pointed out, as Gerlach[11] and Bielschowsky and Unger[12] had done previously, that mesoblastic (meningeal) cells may descend into the medullary groove at the time of the disturbed closure and give rise to intramedullary tumors of mesoblastic or mixed origin.

This hypothesis seems to offer the best explanation for the presence of actively forming cancellous bone in the tumor in this case. The tumor was not connected with the meninges, and there is slight chance that it could have invaded the cerebellum from the meninges. It is likewise improbable that following degeneration in the tumor the connective tissue in the walls of the blood vessels could have given rise to such production of bone. One is thus impelled to suppose that the bone arose from meningeal cell rests included in the medullary tube when it closed early in embryonic life to form the rhombencephalon. The pathogenesis of the tumor would seem, therefore, to be characterized by dysraphia, mesoblastic cell inclusion, ependymal proliferation and the formation of new bone. In this process dysraphia is the earliest and probably the primary manifestation.

This case emphasizes the close relationship between embryologic malformations and neoplasms, which has been a subject of pathologic interest since the days of Cohnheim. In this case the improper closure of the medullary groove was followed by proliferative changes in the cells of the ependymal layer, while bone was formed by mesoblastic cell inclusions. The duplication of the primary ependymal gliosis of syringomyelia in the tumor suggests that, like syringomyelia, it was the sequel of a process of dysraphia. That the ependymoblastoma in this case also duplicates that associated with syringomyelia in the case reported by Mackay and Favill[10] again suggests that a similar condition existed in both instances.

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9. Bailey, Percival: Quelques nouvelles observations de tumeurs épendymaires, Ann. d'anat. path. **2**:481 (Nov.) 1925.

10. Mackay, R. P., and Favill, John: Syringomyelia and Intramedullary Tumor of the Spinal Cord, Arch. Neurol. & Psychiat. **33**:1255 (June) 1935.

11. Gerlach, W.: Ein Fall von kongenitaler Syringomyelie mit intramedulärer Teratombildung, Deutsche Ztschr. f. Nervenh. **5**:271, 1894.

12. Bielschowsky, Max, and Unger, E.: Syringomyelie mit Teratom- und extramedulärer Blastombildung, J. f. Psychol. u. Neurol. **25**:173, 1920.

In this way one sees illustrated several varieties of ependymal proliferation following a developmental malformation of the median dorsal raphe. But the whole ependyma of the nervous system is embryologically a midline tissue, even that in the lateral ventricles, since it is merely the lining of the primitive medullary groove. Hence it is in a position to be disturbed by any malfusion of the medullary crests, or even by less important forms of developmental abnormality. How such dysraphia leads to proliferation is a matter of speculation alone. One might suppose that the developmental disturbance includes displacements of some of the germinal cells of the ependymal layer and that this loss of orientation leads to proliferation. Mesoblastic cell inclusions, as in this case, could only increase such a disturbance. This is in essence, of course, an application of Cohnheim's theory to tissues of ependymal origin. It is my purpose not to indulge in undue speculation but only to emphasize the rôle played by embryologic malformation in this case in initiating proliferative changes and to suggest that it may be a possible factor in ependymal growths wherever they are found.

SUMMARY AND CONCLUSIONS

A case of mixed ependymoblastoma and osteoblastoma in the fourth ventricle is reported.

The proliferation of new bone in the tumor suggests that a process of malformation of the median dorsal raphe (dysraphia) of the medullary tube was a prime factor in initiating the ependymal growth.

Since a similar process probably lies back of the primary ependymal gliosis of syringomyelia, embryologic malformations would seem to be possible factors in ependymal proliferations wherever they are found.

DISCUSSION

DR. R. M. STRONG: Eight years ago an article appeared in *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* (**265**: 1927) in which a bony mass about 2 cm. in diameter was described which was found in the right putamen of a tabetic patient aged 43.

DR. R. P. MACKAY: If formation of bone may occur in tuberculous or syphilitic granulomatous tissues, as has been reported, its occurrence in abscesses of the brain should not surprise one. In such a case, however, the bone must arise from meningeal or perivascular connective tissue and not as the result of an embryologic malformation.

Abstracts from Current Literature

THE ANATOMY AND PATHOLOGY OF THE SUPERIOR CEREBELLAR ARTERY. MACDONALD CRITCHLEY and PAUL SCHUSTER, Ztschr. f. d. ges. Neurol. u. Psychiat. **144**:681 (March) 1933.

In lower vertebrates the cerebellum is supplied by five pairs of vessels known as the arteriae cerebelli (α, β, γ, δ and ϵ). The arteria cerebelli α originates at the caudal portion of the carotid or the basilar artery; it runs behind the oculomotor nerve, skirts around the brain stem and ends in the upper part of the cerebellum and vermis. In fishes, amphibia and reptiles this vessel is small. It is not found in birds. The arteria cerebelli β runs between the pons and the corpus trapezoideum in front of the abducens nerve to the cerebellum; this vessel is particularly important in birds and all vertebrates in which the basilar artery receives blood from the carotid artery. If the basilar artery communicates with the first spinal artery, the arteria cerebelli β is small and does not reach the cerebellum. In such cases the γ branch is well developed.

In mammals there are two chief cerebellar vessels, the anterior and posterior cerebellar arteries, which correspond to the superior and the anterior inferior cerebellar artery of man. The anterior cerebellar artery in mammals is the counterpart of the arteriae cerebelli α and β in lower vertebrates. The corresponding counterparts of the γ, δ and ϵ branches are the posterior cerebellar and the vertebrocerebellar artery. The latter corresponds to the posterior inferior cerebellar artery in man. In apes, the anterior cerebellar artery is insignificant, but the vertebrocerebellar artery is well developed.

The superior cerebellar artery in man takes origin shortly before the branching of the basilar artery and runs parallel with the posterior cerebral artery, from which it is separated by the oculomotor nerve. The arteries surround the midbrain and divide at the edge of the peduncle into two branches which run close to the trochlear nerve. Laterally, at the inferior colliculi the arteries suddenly change their course, running downward and outward. Then they diverge, one taking a lateral and the other a medial course. The lateral branch follows along the ledge of the cerebellum, sending branches to the lateral parts of the lobus centralis and the lobus lunatus anterior and posterior. It ends at the lateral angle of the hemispheres, where it supplies a small part of the lobulus posterosuperior. This artery may be spoken of as the marginal artery. There are two collateral branches: (1) the middle peduncular artery, lying close to the trigeminal nerve, and (2) the floccular branch to the anterior part of the flocculus. The medial branch gives off numerous branches in the vicinity of the colliculi. The main branch runs over the upper surface of the cerebellum and ends in two or three bundles of vessels; the most medial are called the vermicular branches and supply the culmen, the declive and the cacumen; the lateral, or lunate, branches supply the entire upper surface of the cerebellum. Branches of fine network, called the plexus pedunculi, formed from this vessel anastomose with small branches of the posterior cerebral vessel. This is apparently the only place in the brain where vessels of the cerebellum anastomose with those of the cerebrum.

For clinical purposes it is necessary to know the exact distribution of the superior cerebellar artery. This may be divided into two territories: (1) the pons and midbrain and (2) the cerebellum. In the pons and midbrain, the artery supplies a segmental area comprising the colliculi, the spinothalamic tract, the superior cerebellar peduncle, the oculomotor nerve, the substantia nigra and the important tracts to the pons. Most of the pons and the midbrain is supplied by perforating and long and short transverse branches of the basilar artery. How much is supplied by the superior cerebellar artery is hard to determine by injections. Softenings in the distribution of this vessel extend farther than the clinical picture indicates,

including a part or even all of the red nucleus, the substantia nigra, the upper two thirds of the superior cerebellar peduncle, a part of the lateral lemniscus and the trigeminal nucleus.

The cerebellar territory of the vessel includes the cortex and white matter of the entire dorsal cerebellar surface. It includes the lingula, the upper half of the vermis, a part of the lobus centralis, the lobus lunatus anterior and posterior and a part of the posterosuperior lobule.

Clinical reports of pathologic changes in the superior cerebellar artery are not numerous. One of the early reports was that of Mills (1908), who emphasized the combination of ataxia of one side with disturbances of pain and temperature sense of the opposite side. Postmortem study by Spiller showed softening in the left cerebellar cortex, the left cerebellar peduncle and the fillet, as well as in the dentate nucleus. A case of von Schaller (1921) corresponds closely with the anatomic findings in the cases reported by Critchley and Schuster. There was degeneration of the left fillet, the restiform body and the olive, with changes in the left middle cerebellar peduncle and dentate nucleus. There were slight changes in the right dentate nucleus, the middle cerebellar peduncle and the red nucleus. The most important clinical symptoms were asynergia, cerebellar catalepsy and scanning speech. A report by Guillain, Bertrand and Péron (1928) emphasized the cerebellar symptoms of one side and the decreased pain and temperature sense of the opposite side; these authors noted also involuntary movements of the right shoulder and nasal and scanning speech without a disturbance of pharyngeal movements. Necropsy revealed softening of the right cerebellar surfaces, the right isthmus, the cerebellar peduncles and the lateral fillet and atrophy of the right red nucleus. The right corpus restiforme and left olive were atrophied. Worster-Drought and Allan described a case with decrease of all forms of superficial and deep sensation, with loss of power, intention tremor and light wavelike movements on the left side. Necropsy revealed involvement of three vessels: the superior cerebellar artery (bilaterally) and the left anterior cerebellar artery.

Six cases of occlusion of the superior cerebellar artery are reported. In case 1, that of a man aged 61, there were apoplectic dysarthric disturbances, slight paretic difficulties and severe ataxia in the left arm and leg, tremor of both arms and definite sensory disturbances of the left side of the body. Anatomically there was softening in the proximal half of the pons on the right, destroying the entire medial fillet and part of the cerebellar peduncle. There was marked degeneration in the left red nucleus and in the right central tegmental tract. There was retrograde atrophy of the right fillet. Case 2 was similar. The patient, a man aged 62, with a history of syphilis and excessive use of alcohol, had three mild insults and one severe one. He had a slight weakness of the left arm, with spastic reflexes in the left leg, marked disturbance of deep sensation in the left arm, in contrast to intact superficial sensation, mild disturbance of deep sensation in the left leg and severe ataxia of the left arm and leg, and later ataxia of the right arm and leg. There were tremor and adiadokokinesis of the left arm. There were also astasia, dysarthria and compulsive crying. Anatomically there were a large area of softening on the right side in the tegmentum of the pons at the level of the decussation of the superior cerebellar peduncle and a small focus on the left, under the mesial fillet, involving the deep transverse pontile fibers. The lesion on the right side destroyed the mesial fillet, the spinothalamic tract and the basal part of the decussation of the cerebellar peduncle; it injured a small part of the pyramidal fibers, Monakow's bundle and the central tegmental tract. The left focus touched the mesial fillet; the territory destroyed was small, involving only the branches of the superior cerebellar artery to the lateral tegmental portion of the pons.

Case 3, was that of a woman, aged 65, who had a cerebral insult followed by tremor of the left arm and leg. She had marked hypotonia of the left arm and leg, hypotonia of the right arm and leg, asynergia and tremor of the left arm and leg and falling to the left in walking and standing. At first sensation was normal; this was followed by tactile hypesthesia with hyperalgesia in the distribution of the fifth nerve on the right side and later by slight loss of pain sense over

the right side of the body. Anatomically there were a large softening in the left cerebellar hemisphere, diminution in the size of the left cerebellar hemisphere, complete softening of the cerebellar peduncle in the distal part of the pons, disturbance of a large part of the left side of the pons; injury of the left fifth nucleus and of the vestibularis, demyelinization of the right olive and almost complete lack of the right central tegmental tract and less complete atrophy of the left; the left mesial fillet was injured.

In case 4 more than the superior cerebellar artery was involved, part of the anterior inferior cerebellar being affected. Roughly, the softening involved the right side of the pons, the right middle cerebellar peduncle, the junction of the pons and the colliculi, the dorsal surface of the right cerebellar hemisphere and the right lobus biventralis. Cases 5 and 6 were not so striking in their manifestations.

In four of the six cases reported the softening involved the vicinity of the decussation of the superior cerebellar peduncles. Only in two cases was this area free. The cerebellum was involved in only three cases.

Anatomically there were two groups of cases: (1) those in which only the branches to the tegmental region were involved and (2) those in which there was also involvement of the cerebellar branch of this vessel. In three cases the anatomic findings resembled one another closely. The focus was in the proximal part of the pons, where the middle cerebellar peduncle approaches the cerebral peduncle and where both fillets and the spinothalamic tract are present. It seems that the branch of the superior cerebellar artery to the tegmentum of the pons is particularly predisposed to softening. The changes in the central tegmental tract were secondary. The olives were partly degenerated in all cases. The medial fillet was also constantly affected.

Clinically the cases showed a combination of cerebellar and sensory symptoms. These symptoms were sometimes on the same side and sometimes on different sides. They were on different sides in the group of cases in which, besides the pontile softening, there was also softening in the main branches of the artery to the cerebellar hemisphere. They were on the same side in cases in which only the pontile branch was affected. Critchley and Schuster describe a close relationship between central tegmental tract, olives and cerebellum. They believe that the central tegmental tract deals with the acts of walking and standing.

ALPERS, Philadelphia.

THE GROWTH HORMONE OF THE ANTERIOR PITUITARY. H. M. EVANS, J. A. M. A. **104**:1232 (April 6) 1935.

Evans believes that an immense step forward was taken by the experimental production of dwarfism when the pituitary gland was removed from young animals. The classic experiments of Aschner, which were done with puppies with litter-mate controls, showed that an immediate arrest of growth and development was occasioned by the operation. It was conceivable, of course, that the dwarfism following hypophysectomy was a secondary effect, i. e., that it was due to some obscure metabolic upset consequent on loss of the gland rather than the direct outcome of the elimination of a specifically needed substance that could be justifiably called the growth hormone. It was perhaps fortunate, then, that experimental evidence of the existence of the growth hormone had been secured by the production of gigantism in normal animals. The gigantism or accelerated growth that may thus be induced by extracts of the anterior lobe of the pituitary gland in the rat is an extreme one. Obscure but indubitable is the continued need on the part of the body for the growth hormone in adult life. The glands of grown cattle yield proportionately the same amount of growth hormone as do those of rapidly growing young calves. The endocrinologist is already acquainted with the continuous production of blood cells throughout adult life and the replacement of cells lost through attrition at the intestine and surfaces of the skin, but these processes are apparently not significantly impaired in hypophysectomized animals. The distortion of growth in adult life that produces the disease called acromegaly is well

known. The classic explanation of the disorder has been that growth has been imposed on the skull and extremities when stature changes are impossible because of epiphyseal closure. Should one learn to close prematurely the epiphyseal disks of rats, one might hope to make them acromegalic; but there are some serious objections to this simple explanation of the situation. One of the greatest needs in research on the growth hormone is the discovery of a specific biologic test for the hormone that can be rapidly performed. At the present time two reliable tests are known and are employed in the detection of the growth hormone. They are done by the use of adult normal female rats or hypophysectomized rats of either sex. Even though growth deficiency often seems the sole outstanding defect, in all cases of dwarfism the output of other hypohyseal hormones may be subnormal, and it is probable that future research will establish that medication with more than a single hormone is indicated. Recent biologic experimentation itself has begun to speak decisively for the improvement of growth when in addition to the growth hormone other hormones are concurrently administered. There is no information yet as to whether the growth hormone acts directly on the widespread tissues of the body which it stimulates to increase. The improved appetite of normal animals under the influence of the growth hormone is always strikingly evidenced by the increased consumption of food, but the unusual growth produced by the growth hormone is not referable to so simple an explanation. The exact mechanism of action of the growth hormone on metabolism remains entirely unknown, but a significant beginning has been made in the analysis of its effects. The study of Lee and Schaffer showed that treated animals do not possess the characteristic age changes that normal rats exhibit (decreases in the proportion of water, nitrogen, fat-free dry tissue and ash, and increases in the percentage of fat) but retained with considerable exactitude their initial composition in certain chemical constituents. This propulsion of growth in the rat's adult life is therefore associated with the retention of certain juvenile chemical characteristics in the tissue produced, and the question naturally arises as to whether the "youthfulness" of this tissue indicates "youthfulness" of the animal with regard to expectance of a correspondingly longer life span. Other studies, such as those of the physiologic performance of such animals, have not yet been made. Possible changes in the mental acuity of animals forced to continue maximal growth have not as yet been investigated. The growth hormone is probably itself a protein or so closely associated with protein as to make its separation from protein extremely difficult. The purest forms of it heretofore available when analyzed continue to contain about 16 per cent of nitrogen and to give most of the classic qualitative tests for protein. For extracting the hormone from anterior lobe tissue, all workers continue to employ dilute aqueous alkali, the method originally introduced by Evans and Simpson. The problem of preliminary purification resolves itself into separation of the hormone from the greater part of the contaminating protein with which it is associated.

EDITOR'S ABSTRACT.

THE REPRESENTATION OF THE MESIAL SECTORS OF THE RETINAS IN THE CALCARINE CORTEX. GORDON HOLMES, Jahrb. f. Psychiat. u. Neurol. **51**:39, 1934.

Holmes reports the case of a man, aged 47, with bilateral blindness which involved the whole of each visual field except small areas in the region of the fixation points and sectors on each side of the superior vertical radii of the fields. The absence of changes in the retinas and in the media of the eyes, adequate to explain the loss of vision, and the absence of lesions in the optic nerves, chiasm, optic tracts and radiations as well as the congruity of the defect in the two fields left no doubt that the loss of vision was due to cortical lesions. On the other hand, histologic examination of the brain in serial sections disclosed extensive but relatively superficial destruction of the cortex and white matter in the region of each calcarine fissure, the result of occlusion of those branches of the posterior cerebral artery and especially of the calcarine artery which supply this part of the brain.

Holmes points out that in pathologic processes in man the usual problem is the correlation of negative or defect symptoms with destructive lesions of the nervous system, a problem often complicated by difficulties which are frequently overlooked. A safer mode of approach, therefore, to the problem is to attempt to explain the remaining vision in terms of those parts of what is assumed to be the visual cortex that escaped damage from the extensive softenings in both occipital lobes. To state the problem in other words: The retention of vision in certain portions of the homonymous halves of the visual fields necessitates the existence of functioning cortex in the opposite cerebral hemispheres and of intact afferent fibers to this cortex. The extent to which the optic radiations may have been affected is therefore of little significance unless an exact quantitative correlation of the intact portions of the visual fields with the extent of the remaining visual corex is attempted, and that is not within the scope of this contribution.

The retention of central vision can be related to the partial sparing of each occipital pole, for there is no question that macular vision is localized at the posterior extremities of the areae striatae. In the right hemisphere a considerable portion of the cortex of the occipital pole was intact below the level of the calcarine fissure and a smaller amount above it. The charts of the visual fields disclosed a small area of vision below and to the left of the fixation points, while above the fixation points vision extended to the normal periphery. This is precisely what would be expected from the results of histologic examination if macular vision is represented at the posterior extremity of the area striata and if the lower portions of the retinas are projected on the lower portion of the visual cortex.

Unfortunately, the left occipital pole was not available for examination, but at necropsy the amount of normal calcarine cortex at the posterior end of the occipital pole was found to be smaller than on the right, and it lay chiefly below the area of softening. The greater extent of the area of softening in this hemisphere may correspond with the smaller areas of vision remaining at the right of the fixation points.

The only vision otherwise remaining in the right halves of the fields occupied a sector between the upper vertical radii and at the radii at 45 degrees from them. Anatomic examination revealed that only the lower margin of the left area striata, and chiefly the part lying on the exposed surface of the lingual gyrus, was intact. This, according to Holmes, is strong evidence that the mesial sectors of the upper quadrants of the visual fields are represented in the lower margin of the area striata. This conclusion is confirmed by examination of the right cerebral hemisphere, for here too only the lower part of the area striata was unaffected, except for a small island in the cuneus which was isolated and probably functionless, whereas vision was preserved only in the corresponding mesial sectors of the left upper quadrants. In this connection it is interesting to note that the area of intact cortex was somewhat greater in the right hemisphere than in the left, while a larger area of sight was present in the left halves of the visual fields.

This case, therefore, presents further evidence not only that the lower halves of the retinas are represented in the lower parts of the visual cortex but that the vertical sectors of the retinas are projected mainly on to those portions of the calcarine cortex exposed on the mesial surfaces of the hemispheres.

KESCHNER, New York.

PHYSIOPATHOLOGY OF NYSTAGMUS OF THE HEAD IN MAN. J. ROTHFELD, Rev. d'oto-neuro-opht. **12**:481 (July-Aug.) 1934.

A man, aged 40, an excessive smoker and drinker, with no history of previous illness, entered the clinic with the complaint of peculiar movements of the head that had existed for the preceding year. Five years previously he had an attack of encephalitis. When he was in the upright position the head was bent forward, turned and inclined to the left shoulder; nystagmic movements (quick phase toward the left) at the rate of 100 per minute were observed. When he lay on the left side or the back the movements became less or ceased; when the head was

turned to the right the movements were the same as when the head was upright. The nystagmic movements disappeared for an instant when the finger was placed on the forehead, or even before the finger touched the patient. There was no ocular nystagmus. Labyrinthine stimulation produced normal responses and did not influence the cephalic nystagmus. The patient presented a distinct parkinsonian aspect. Occasionally forced movements of the eyes upward were observed. The Wassermann reaction of the blood was negative.

Nystagmus of the head in man is observed only in pathologic states; it has been seen in disease of the labyrinth with a fistula in the semicircular canals. Rosenfeld observed it in a case of multiple cerebral softening; douching the ear with cold water and rotation caused nystagmus of the head, which corresponded with the ocular nystagmus, but galvanic stimulation did not cause it. Woolsey observed vertical ocular and cephalic nystagmus in a case of multiple sclerosis. Kannibayshi reported a case occurring during acute otitis interna and meningitis. Kragh observed nystagmus of the head and trunk during labyrinthine stimulation in a patient with headache and vertigo. These were the only cases found reported in the neurologic literature.

In Rothfeld's experiments, ablation of the frontal lobe, the striate body and the anterior part of the thalamus resulted in abolition of the rapid phase of cephalic nystagmus toward the sound side after rotation toward the side on which operation had been performed; the slow component was retained. After rotation to the sound side complete cephalic nystagmus was present. A bilateral lesion caused loss of the quick phase after rotation toward either side. Destruction of the whole thalamus resulted in the loss of both phases of cephalic nystagmus. The deduction is that the center for the quick phase of cephalic nystagmus lies in the anterior part of the thalamus; that for the slow phase is situated in the posterior part. The latent base for nystagmus movements of the head is indispensable for the production of the rapid phase of cephalic nystagmus; if the slow phase is absent the rapid phase cannot be produced, although the part of the thalamus or striate body corresponding to the rapid nystagmic movement is preserved. These experiments reveal the existence of an intimate relation between the vestibular apparatus and these subcortical centers. All bulbar lesions are characterized by a pathologic position of the head toward the opposite side, absence or diminution of the reaction after rotation toward the opposite side or toward either side and an absence or diminution of the falling reaction toward the healthy side. In lesions of the cerebral trunk there are also an abnormal position of the head (but it is toward the sound side), spontaneous falling toward the sound side and a more marked reaction of falling toward the sound side.

In comparing the cases of Rosenfeld, Woolsey and Rothfeld, it is clear that a different central mechanism must be postulated in each case. In all three, however, there must exist, aside from the subcortical lesions, lesions of the centers of the vestibular nerve in the bulb or in the pathways connecting these centers with the subcortical centers. In Rosenfeld's case lesions were present both in the subcortical centers and in the pons. Clinically, the cases of Woolsey and of Rothfeld justify the assumption of similar lesions. It appears doubtful that a fistula of the labyrinth alone is sufficient to produce cephalic nystagmus following labyrinthine stimulation. In such cases a neurologic examination may make clear the physiopathology of the phenomenon.

DENNIS, San Diego, Calif.

BLINDNESS AND PAPILLEDEMA IN GUERNSEY CALVES. G. E. DE SCHWEINITZ and PERCE DE LONG, Arch. Ophth. **11**: 194 (Jan.) 1934.

This is the second communication on this subject and it continues the study started by de Schweinitz. An abstract of the first article also appeared in this journal (Blindness and Papilledema in Guernsey Calves, Usually Bulls, ARCH. NEUROL & PSYCHIAT. **28**: 710 [Sept.] 1932). The disease is regarded as a clinical entity, well known to veterinarians and others concerned with the care of cattle, but one to which comparatively few publications have been devoted. It was first

carefully described, apparently, from general and pathologic standpoints, thirty years ago, by Nettleship and Hudson; it is characterized by complete blindness and papilledema (choked disk), practically unassociated with other symptoms; it exists among calves (male and female), usually (if not exclusively) of the Guernsey breed, and is generally detected within the first year of life; it may be present at birth. The important pathologic lesions revealed by this research were: enlargement of the optic disk, depending on marked increase in its neuroglia and swelling of the cell bodies; atrophy of the nerve elements of the optic nerves, the optic tracts and the chiasm; marked degeneration of the retinal ganglion cells, and no gross intracranial lesions but with definite edema of the cerebral hemispheres.

The present communication is concerned with the investigation of another blind Guernsey calf examined by de Schweinitz five days after birth. The calf had been born totally blind and was admitted to the hospital of the veterinary department of the University of Pennsylvania on the fifth day. A complete ophthalmologic examination was made and is reported in the paper.

The calf was killed with chloroform, and autopsy was performed. Microscopic sections revealed papilledema and almost complete atrophy of the optic nerve fibers. The gross anatomic study showed the animal to be normal throughout. The optic nerves and the optic tracts were studied microscopically. All other organs, including the cerebellum and the spinal cord, were normal. There may have been slight fibrosis of the meninges. The medulla oblongata showed slight congestion and edema with a few minute pericapillary hemorrhages, which may have been the result of the method of putting the animal to death and were not regarded as of pathologic importance.

From the paper in general and the authors' conclusions, the following points may be briefly summarized. A certain form of permanent blindness is not uncommon in pedigreed male and female calves, the animals being otherwise apparently normal. The ophthalmoscopic signs of this condition are: papilledema alone or papilledema associated with patches of choroiditis and occasionally with small hemorrhages. There is extensive atrophy of the optic nerves, optic tracts and chiasm. The continuity of the optic nerves was interrupted incidentally by a block of fibrous tissue. The cerebral hemispheres revealed edema which might have caused an increase of intracranial pressure and have been responsible for the papilledema. It is probable that the lesions always begin in prenatal life, and that blindness may be present at birth or cannot be detected for months after birth. It is also probable that the lesions cannot reach a maximum until a number of months after birth. Apparently a blind animal, whether dam or sire, does not transmit the blindness to its progeny as a dominant feature, though thus far the opportunity has not arisen to ascertain whether, if both dam and sire were blind, the blindness would be transmitted to their offspring. It is probable that this form of blindness may be regarded as a special or familial disease (similar to Leber's disease in man), which depends largely on inbreeding for its origin, whereby two "recessives" come into contact.

SPAETH, Philadelphia.

FAMILIAL CHARACTERISTICS OF THE CEREBRAL SULCI AND CONVOLUTIONS IN SCHIZOPHRENICS. A. D. ZARUBASHVILI, Coll. Papers Bechterew's State Inst. Study Brain, Leningrad **2**:175, 1934.

Zarubashvili investigated the possible presence of familial morphologic resemblances in the brains of two brothers and two sisters who died in the Third Leningrad Psychiatric Hospital while suffering from schizophrenia. The investigation was carried out along the lines of studies previously made by Richter and Karplus. The latter reported in 1907 the results of his classic study of eighty-six hemispheres; he concluded that "there exists an inheritance of cerebral sulci." He also believed that the transmission of the inherited characteristics is homolateral in nature. Pines, who studied the brains of the academician Bechterew and his brother, found both homolateral and contralateral resemblances of the sulci. Zarubashvili paid particular attention to the location, course, form,

branching, character of anastomoses, interruptions and duplications of the sulci. He first investigated the individual symmetry, that is, the symmetry of the hemispheres in an individual brain. A comparison of the same sulci in the hemispheres of the brothers revealed symmetry of only a few sulci on the mesial surface of the hemispheres, especially of the sulcus cinguli, the parieto-occipital fissure, the sulcus rostralis and the sulcus rostralis inferior. No such individual symmetry of the sulci was observed in the hemispheres of the sisters. The author considers complete and partial similarities; under the latter term he understands slight variations in otherwise essentially similar sulci. Each sulcus was compared with the same sulcus in both hemispheres, thus giving four combinations. The parieto-occipital and the calcarine fissures in the hemispheres of the brothers showed a close similarity in all four combinations, homolaterally as well as contralaterally. The sulcus cinguli in the right hemisphere revealed a certain resemblance to its homolateral homolog. In both brains the sulcus cinguli consisted of two parts; in one of the brains, however, the anterior part was twice as long as in the other brain. The sulcus cinguli of the left hemisphere of one brother was identical with the same sulcus in the right hemisphere of the other sibling. The sulcus rostralis and sulcus rostralis inferior showed a fairly good similarity in all four combinations. The homolateral subparietal sulci were quite alike as to the character of their parts and number. The central sulci of Rolando looked alike in their course and the form of their curves in all hemispheres. The upper precentral sulci showed a complete homolateral similarity in both brains. The lower precentral and the frontal lower sulci showed good resemblance as to position, direction and anastomoses in the contralateral comparison only. The postcentral right homolateral sulci were identical, while the homologs on the left side showed slight variations.

In the encephalons of the sisters there was a complete resemblance of the parieto-occipital fissures and of the calcarine fissures in contralateral comparisons. Similarly, the sulcus cinguli showed only a contralateral resemblance, while the subparietal sulci were all fairly identical. The rostral sulci revealed a complete homolateral and a partial contralateral similarity. There was also a homolateral resemblance of the central inferior precentral and the interparietal sulci. Finally, the collateral fissure showed a right homolateral branching with an identical accurateness into two limbs in both brains.

The author does not attempt to draw definite conclusions from his study for the time being, believing that his material is too limited for such a step.

NOTKIN, Poughkeepsie, N. Y.

PSYCHIATRIC STUDY OF HYPERTHYROID PATIENTS. AGNES CONRAD, J. Nerv. & Ment. Dis. **79**: 505 (May); 656 (June) 1934.

A history of psychic trauma was obtained in 94 per cent of 166 women and 34 men with exophthalmic goiter by a method of examination stressing: (*a*) the investigation of new developments in the life situation and personal relations at the time of the onset of the symptoms of hyperthyroidism and (*b*) the evaluation of the unconscious conflicts by the appearance of signs of emotion during the taking of the history. The flushing of the neck and of the lower part of the face is described as showing a high degree of specificity in leading one to the discovery of the conflict which has caused the patient to become "decompensated." The flushing is frequently noted in mild form, if the patient is interviewed in a good light, and the degree of severity shows some correlation with the elevation of the basal metabolic rate and also with the violence of the trauma recalled. Though all degrees of variation in intellectual and economic self-reliance were observed among the women, the majority showed great dependence emotionally on the mother or mother surrogate and found any threat to such protecting mother-care or to approval by the mother intolerable. Another group was unable to bear the burden of maternal responsibility, such as the nursing of dependents. In some cases both these patterns appeared; in others there was no trace of one but a clear instance of the other. A small number of

the women showed fear of coitus, fear of pregnancy and delivery and fear of specific illness, among which heart disease and cancer figured conspicuously, though in most instances these seemed terrifying because they were feared by, or were fatal to, a mother-person.

The men also showed fear of deprivation of mother-comforts, but the fear of loss of approval was less specific, appearing as fear of public disgrace. The fear of illness included fear lest the wife suffer, as did the mother, from disease, economic neglect or unwanted pregnancy.

The emotional pattern of these personalities may be explained by the formulation of a pathologic development, often a frustration in the normal attempt to establish independence of the mother. In uncomplicated cases of exophthalmic goiter the relation to other people shows no pathologic change, whereas this also is involved in cases in which there is associated hysteria or paranoid tendency.

It seems, therefore, from the incomplete study made that the conception of exophthalmic goiter must be extended to include susceptibility to specific emotional traumas and a characteristic personality pattern. Many patients with hyperthyroidism showed endocrine imbalance in their development, anamnesis and family history. The body form of the men and in a less striking number of cases of the women showed hypogonadal development. Adaptation to other people was normal; on the whole the patients seemed to make friends easily.

Indication is for therapy to be directed toward increasing both the stability of autonomic functions (as by partial thyroidectomy) and the self-confident independence of the personality. So far as this is impossible of expectation the maximum of physical and emotional shelter becomes imperative. Insight into the specific threats to which each patient is sensitive aids in the establishment of security from within and from without. Conrad does not compare this group with a corresponding group of so-called normal persons without symptoms of hyperthyroidism.

HART, Greenwich, Conn.

THE VENOUS SYSTEM OF THE VELUM INTERPOSITUM OF THE RHESUS MONKEY AND THE EFFECT OF EXPERIMENTAL OCCLUSION OF THE GREAT VEIN OF GALEN. T. H. BEDFORD, Brain **57**:255 (Oct.) 1934.

In a previous investigation (1934) Bedford studied the effect of experimental occlusion of the great vein of Galen in dogs. He found that after a survival period of three months none of the animals at autopsy showed hydrocephalus. He also studied the venous system of the velum interpositum of these dogs and found it to differ from that of man. The present communication deals with a similar study in the rhesus monkey. The striking feature of the galenic system in the rhesus monkey is its remarkable irregularity and variability. It seems to be even more variable than in the dog. The vein of the choroid plexus receives blood from the choroid plexus of the lateral and third ventricles. Soon after leaving the choroid plexus it is joined by a tributary which receives blood from the anterior part of the corpus callosum. After pursuing a course backward through the velum interpositum for a variable distance, the vein of the choroid plexus unites with the vein of the corpus striatum to form the vein of Galen. The veins of Galen run backward until they reach the region of the splenium of the corpus callosum where they unite to form the great vein of Galen. The latter vessel turns upward round the splenium and ends by becoming the straight sinus at the anterior border of the tentorium cerebelli. Two pairs of tributaries are usually received by the great vein of Galen near its origin. One pair Bedford calls the epithalamic veins because they appear to drain blood mainly from the surface of the posterior part of the optic thalamus. The vessels usually terminate in the great vein of Galen near its point of origin, but they have also been observed to end in the vein of Galen, the basilar vein and the under-surface of the great vein of Galen close to the point where it becomes the straight sinus. The other pair is composed of the basilar veins, which are formed by the union of the anterior cerebral vein and the sylvian vein. In twelve animals studied by Bedford the basilar veins were found to

terminate in a different manner, ending most frequently in the lateral sinus. In this respect the system resembles that of the dog, in which this mode of termination of the basilar vein is constant.

The great vein of Galen was experimentally occluded in nine monkeys. In five the health was good for six weeks, and the experiments were considered as successful. None of the animals in which the great vein of Galen had been occluded showed hydrocephalus, and in most instances the ventricles appeared to be somewhat collapsed. One of the most striking features of the galenic system in these cases was the absence of any clear indication of the manner in which collateral circulation had developed. Except for the presence of the occluding clip, the whole system appeared to be normal. Bedford states that it was unfortunate that the method employed for preparing the brains prevented rapid fixation of the choroid plexuses, as they were rendered unsuitable for histologic examination. However, the choroid plexuses remained unchanged in gross appearance. Bedford considers the possibility that although there is no main channel through which collateral circulation is established, the escape of blood may be a general process through the communications of the minute tributaries of the occluded vessels with those of the veins of neighboring systems. This aspect of the subject, he states, requires further investigation.

SALL, Philadelphia.

THE PUPILLARY CHANGES IN PATIENTS WITH DEMENTIA PARALYTICA UNDER THE INFLUENCE OF MALARIA TREATMENT. K. OHYAMA, Folia psychiat. neurol. japon. **1**: 1 (Dec.) 1933.

Ohyama first reviews the scanty reports in the literature on the favorable influence of the various types of therapy on the pupillary light reaction in cases of dementia paralytica. He refers especially to the reappearance of the reaction following mercurial inunctions as reported by Bumke and following arsphenamine therapy as reported by Zaun, Igersheimer, Last and others. His own original report following inoculation with malaria was made in 1930. Since then, improvement in the pupillary light reaction with malaria treatment was reported by Gerstmann, Nonne, Kirschbaum and Weygandt. Ohyama criticizes, however, the method used in these studies, pointing out the possibility of errors in a simple inspection of the pupil with the unarmed eye. He further emphasizes the importance of the subjective element and of the difficulty in evaluating the difference between a sluggish reaction prior to treatment and a modified but still pathologic response following therapy. He points out that the only gross observation that can be accepted without risk of error is a change from a static pupil before therapy to a pupil that definitely contracts following therapy. For accuracy, therefore, he uses the Hess differential pupilloscope, which enables him to measure quantitatively the "difference of the motor sensitivity" (*motorische Unterschiedsempfindlichkeit*).

Sixty-two of 72 patients with dementia paralytica who had static pupils prior to inoculation with malaria showed no improvement in the pupillary light reaction after treatment. In only 4 was there a return of the reaction in both eyes, and in the remaining 6, in only one eye.

In another group of 108 patients with a reduced but still measurable reaction before inoculation with malaria, there was an improvement in 34, a change toward the worse in 42 and no change in the remaining 32. In a few instances the first pupilloscopic readings immediately after therapy gave a diminished sensitivity difference, only to show a progressive and permanent improvement a few days later.

Summarizing the results obtained in the entire group of 180 patients, Ohyama found an improvement in the pupillary light reaction in 24.5 per cent, and no change in 52.2, while in the remaining 23.3 per cent the pupillary light reaction became worse. He also attempts to correlate the changes in the mental state with that in the pupillary reaction. There was an improvement in the pupillary reaction in 43.6 per cent of 29 patients with complete remissions, in 21.9 per cent of 73 patients with partial remission, and in only 16.2 per cent of the remaining 68

in whom the clinical condition remained stationary or took a downward course. The author draws the conclusion that there is a certain parallelism between the mental state and the pupillary light response and that inoculation with malaria often influences the pupillary changes. He closes his article with a suggestion of the existence of a phase of functional pupillary disturbance prior to the complete destruction of the pathway of the light reflex.

NOTKIN, Poughkeepsie, N. Y.

THE EFFECT OF NON-SEDATIVE DRUGS AND OTHER MEASURES IN MIGRAINE WITH SPECIAL REFERENCE TO ERGOTAMINE TARTRATE. SAMUEL BROCK, MARY O'SULLIVAN and DAVID YOUNG, Am. J. M. Sc. **188**:253 (Aug.) 1934.

The authors have investigated the effects of nonsedative drugs and other measures in a group of persons suffering from typical long-standing, severe and intractable migraine. There were nineteen women, aged from 19 to 64, and six men, aged from 36 to 48. The duration of the disease in both groups averaged twenty-one years. The headaches occurred from two to twelve times a month. Menstruation was a provocative factor in thirteen of the nineteen women.

In the authors' series no consistent artificial measure for inducing the headache was found. The administration of the gonadotropic principle of the urine of pregnant women, histamine and large doses of an estrogenic substance were sometimes successful. Hyperpnea was without effect.

In the relief of headache, the most striking benefit was obtained by the hypodermic injection of ergotamine tartrate, a drug which is believed to produce vasodilatation by paralyzing the sympathetic innervation. In this series, eleven women were benefited twenty-seven times, and three men were benefited seven times. Two women were not relieved during the course of three headaches, and two men were not helped during the course of two headaches. At no time was a headache made worse. Once headache had been removed by this drug, a headache was always eased by it. If the drug failed on the first injection, it was ineffective on future trials. Injection of from 0.5 to 1 cc. (0.25 to 0.5 mg.) of ergotamine tartrate caused the headache to disappear in from one to three hours. Vomiting frequently accompanied relief. The authors found subcutaneous administration more effective than oral.

Measures supposed to induce vasodilatation of the cerebral vessels did not give invariable relief. Thus acetylcholine, a parasympathetic (vagus) stimulant, did not always prove helpful, though it gave striking relief in a few cases unaffected by ergotamine tartrate. Histamine was observed to produce cerebral vasodilatation in a man during the course of a cerebral operation (Weiss, Robb and Ellis), yet it was not of benefit in this series; this drug was more apt to intensify or to provoke the pain. Amyl nitrite, another vasodilator, failed more often than it brought relief. Epinephrine also was often of no benefit. While this drug causes dilatation of the pial blood vessels in animals as a secondary result of the rise in blood pressure, it is not known what effect subcutaneous injection of this drug has on the human cerebral circulation.

The administration of the ovarian follicular hormone, which is known to be lacking in women with migraine, did not give the expected results. The intravenous injection of calcium preparations was also more or less ineffective.

The authors conclude that the diversity of results points to the presence of more than one pathophysiologic mechanism in the production of migrainous headache. They were led to believe that vasospasm is probably a secondary effect of, and not a primary factor in, migraine.

WATTS, Philadelphia.

A CONTRIBUTION TO THE STUDY OF PICK'S ATROPHY. R. LEMKE, Arch. f. Psychiat. **101**:622 (Feb.) 1934.

The study reported here was made with special reference to the problem of the relationship of Pick's disease to the senile syndromes. The case studied was that of a man who came under observation four years before death. He was

50 years of age at the time of admission to the hospital. The family history was without significance. The man had been well adjusted and seems to have had no difficulties of any type until two years before admission. At that time he began to show signs of impaired judgment; six months before admission he was dismissed from his position as manager of an industrial plant. On admission there was definite intellectual deterioration, affecting primarily the higher faculties of judgment. He seemed to have lost interest in work as well as in his surroundings, but otherwise he showed no definite impairment. Physically there was slight weakness of the left side of the face and the knee and achilles tendon reflexes were somewhat stronger on the right than on the left. Encephalography showed definite atrophy of both frontal lobes, especially at the poles, and the ventricles were somewhat larger than usual. The patient was studied in the clinic for four years. He presented definitely progressive intellectual deterioration which affected primarily judgment and attention. Memory seemed to be only secondarily involved, mainly because of lack of attention. There was a progressive loss of communication; he would not answer most questions and tended to perseverate in his answers. When left to himself he exhibited a pronounced tendency to hyperactivity of a disorganized type. This continued until shortly before death, when he had two spells of unconsciousness at short intervals. Following the second period bronchopneumonia developed, which was the primary cause of death. Autopsy revealed marked atrophy of both frontal and parietal lobes, which did not, however, involve the anterior and posterior central convolutions. Histologically, the grossly atrophied regions showed shrinkage of the cortex, various stages of degenerative changes of the nerve cells and their replacement by glial tissue. There were no signs of Alzheimer's fibrillary changes and no senile plaques. The vessels showed no arteriosclerotic or inflammatory changes. The myelin stains revealed pronounced disappearance of the myelin sheaths and to a certain extent of the axis-cylinders. The basal ganglia were definitely diseased, showing cellular degeneration and glial proliferation. In discussing this case and other cases of Pick's atrophy reported in the literature, the author comes to the conclusion that there is no evidence to support the view that this disease is in any way related to the group of senile degenerations. He is of the opinion that it belongs to a special group characterized by degenerative changes and showing a special type of clinical picture.

MALAMUD, Iowa City.

THROMBOSIS, EMBOLISM, AND THEIR TREATMENT. GEORGE BANKOFF, Brit. M. J. **1**:189 (Feb. 3) 1934.

Scientists are divided into two main groups in their opinion as to the cause of thrombosis. According to one group it is due to bacterial infection, and according to the other, to a special constitutional predisposition. In Bankoff's opinion, it cannot be denied that infection may be a direct cause of thrombosis. On the other hand, one cannot agree with the supporters of the germ theory who believe that thrombosis is due only to infection. By hypodermic injection of thyroxine, Bankoff is able to divide persons into two major groups, and on this basis he is able to determine those who are susceptible to thrombosis and those in whom it can never occur. The one group is designated as "thyroxine-sensitive" and the other "thyroxine-resistant." In the first group, three hours after 1 cc. of thyroxine is injected hypodermically the pulse quickens, the temperature rises slightly, and differences in the composition of the blood are noticeable; the number of red corpuscles increases slightly, while the number of blood platelets decreases. After two or three injections of thyroxine, these features become two or three times more abnormal, and the time necessary for coagulation of the blood is longer. In the second group, after the same injection it is impossible to detect any changes in temperature, in the pulse rate or in the composition of the blood. To these patients every operation will bring the danger of thrombosis.

The scientific explanation may be that thyroxine acts on the vegetative nervous system and at the same time directly affects the cardiovascular system, producing

the clinical symptoms in the patient. In the thyroxine-resistant group, the effects of the injection are almost unnoticeable because the systems mentioned show little reaction. In this group of patients the parasympathetic nervous system predominates, thus facilitating the formation of thrombosis.

After the effect of thyroxine has been discovered, those susceptible to thrombosis may be treated by the hypodermic administration of a combination of atropine and racemic ephedrine in the proportion of 1/100 grain (0.00065 Gm.) of atropine to ¼ grain (0.016 Gm.) of racemic ephedrine. Not less than three injections are given every other day, beginning on the fifth day after the operation. Not one patient treated in this way has suffered from thrombosis or embolism. Bankoff thinks that in small hospitals it is advisable to treat all patients belonging in the group susceptible to thrombosis. The injection of atropine and racemic ephedrine can never be harmful to the patient and is even useful for the prevention of post-anesthetic pulmonary disturbances.

FERGUSON, Niagara Falls, N. Y.

THE PRESENT STATE OF SURGICAL PROCEDURES ON THE HYPOPHYSIS. M. C. CAVINA, Ann. d'ocul. **170**: 691 (Aug.) 1933.

After a brief outline of the anatomy, physiology and pathology of the hypophysis and their relation to surgical procedures on this gland, Cavina discusses the principal symptoms which indicate excision of the diseased gland. The indications are limited to hypophyseal tumors (within and above the sella turcica) and to certain chiasmal syndromes which are probably due to a toxic condition of the pituitary gland and which were first described by Cavina. Cavina then discusses the proposed surgical methods for the removal of the hypophysis. After having criticized each one of these methods, he indicates the advantages and the disadvantages of those most commonly used.

The most important part of the report is the explanation of the results so far obtained in neurosurgery. By means of statistics, Cavina demonstrated that the rate of mortality and recurrence is very low in operations performed by skilled neurosurgeons. He also states that in a high percentage of the cases visual acuity is restored to normal; in a fairly high percentage there is a marked recovery of vision, and in few cases there is slight or no recovery. Retrogression or improvement of the phenomena of altered nutrition also occurs in a small percentage of cases.

Radiotherapy of hypophyseal tumors is also considered. This method was introduced into Italy in 1908, by Gramegna of Turin. He stresses its value for slowly growing neoplasms which are particularly sensitive to radium. Cavina believes that it is also a valuable adjunct to surgical treatment. In conclusion, Cavina stresses the importance of surgical measures in the management of hypophyseal tumors. Many patients have completely or partially recovered vision after surgical treatment.

BERENS, New York.

THE POTENTIAL EPINEPHRINE CONTENT OF THE ADRENAL GLANDS. G. MOURIQUAND, A. LEULIER and L. REVOL, Rev. franç. d'endocrinol. **2**:324 (Oct.) 1933.

In 1926, Mouriquand and Leulier found the epinephrine content in the adrenals of guinea-pigs immediately after death to be much lower than that detected twenty-four hours later. They ascribed the increase in the hormonal content to the "ripening" of the gland. They therefore distinguished the free epinephrine, which is detectable immediately after the death of the animal, from the potential fraction which is liberated later. Mouriquand, Leulier and Revol have found further that the increase in the epinephrine content after the animal's death takes place only when the free epinephrine is left intact in the gland. To hasten the liberation of epinephrine, the glands are submitted to a temperature of 85 C. for twenty minutes, or to a temperature of 0 C. or to a dry atmosphere at a normal temperature.

The authors deny Abelous' claim that epinephrine is secreted in the cortex. They admit the possibility of the inclusion of islands of chromaffin cells in the

cortex, which may explain the presence of minimal quantities of epinephrine in the cortical tissue. They have shown that the ripening takes place in the medulla in 90 per cent of the tests, while the reaction is positive in the cortex in only 17 per cent of the tests. They speculate as to the mechanism of the liberation of the so-called potential epinephrine, suggesting the possibility that this process is one of oxidation or flocculation. They have further found that tetanus toxin affects little, if at all, the content of potential epinephrine, while diphtheria toxin and inanition deplete it entirely. In the cadaver complete destruction of both the free and the potential epinephrine occurs. The authors therefore recommend the use of fresh glands of healthy animals for glandular therapy.

NOTKIN, Poughkeepsie, N. Y.

PARALYSIS AGITANS, PARKINSONISM AND TRAUMA. M. SECKBACH, Monatschr. f. Psychiat. u. Neurol. **86**:37 (June) 1933.

Whether a parkinsonian syndrome can be produced solely by trauma is still a subject of dispute. An affirmative answer can be given conclusively only by cases in which all possibility of latent paralysis agitans or a previous attack of epidemic encephalitis can be eliminated. It is therefore necessary to reject all cases in patients over the age of 40, as well as those in which there is a history of encephalitis. One should even exclude cases with a history of influenza during years in which epidemics of encephalitis are known to have occurred. Most of the cases recorded in the literature cannot be regarded as examples of traumatic parkinsonism because the patients were elderly and may well have had arteriosclerotic changes or paralysis agitans in a latent form prior to the injury. Seckbach reports a case in which none of the aforementioned objections were encountered. A woman, aged 27, who had always been healthy, received an injury to the head in May 1929. She was unconscious for a short time and remained in bed for ten days. She then resumed her previous occupation, but four or five weeks later it was noted that all her movements were performed slowly. There were also some slowness of speech and difficulty in talking. The symptoms gradually increased, and gross tremors of the upper extremities appeared. The patient soon had to give up work. Her condition grew worse until 1930 but remained stationary thereafter. Examination three years later disclosed a typical parkinsonian syndrome. There was no question of compensation in the case. Seckbach thinks that the symptoms were probably caused by damage to the pallidum. Since the pallidum possesses a relatively poor circulation, an injury may produce stasis with hemorrhages and later degenerative changes in that nucleus, as a result of which a parkinsonian syndrome develops.

ROTHSCHILD, Foxborough, Mass.

OCULAR AND CEREBELLOVESTIBULAR SYMPTOMS IN THE ANGIONEUROTIC EDEMA OF QUINCKE. LUDO VAN BOGAERT, Rev. d'oto-neuro-opht. **12**: 321 (May) 1934.

This discussion is based on two cases. In one the patient exhibited a serious cerebellovestibulospinal syndrome (horizontal nystagmus, violent vertigo accompanied by nausea, vomiting and falling, adiadokokinesis on the left, increased reflexes in the lower limb and clonus of the left foot) during an attack of angioneurotic edema. The syndrome lasted forty-eight hours and was not repeated. The second patient was a woman with slight insufficiency of the thyroid; long after the menopause and at the time when asthma of seven years' duration disappeared under iodine therapy, crises of angioneurotic edema appeared; this was soon accompanied by true seasonal ophthalmoplegic migraine. In the intervals between the crises, enophthalmia with myosis and diplopia in certain positions of the eyeball and slight facial edema remained.

The association of angioneurotic edema with epilepsy and with hyperthyroidism has been observed, but Foster Kennedy in 1926 was the first to study the cerebral manifestations of angioneurotic edema. The point of great interest in his observations was that he was able to follow the local evolution of the edema

in the vitreous humor. Cerebral urticaria may be manifested by hemiplegia, convulsions, hemianopia, optic neuritis, violent headaches, torpor, pontocerebellar or cerebellar disturbances or disorders of the cranial nerves. The alternation of the manifestations in the brain and in the skin seems to indicate that the neural ectoderm has a certain allergic power. The second case confirms the hypothesis of Buscaino that disturbances of the thyroid are at the base of sensitized states, of which epilepsy is one of the manifestations. DENNIS, San Diego, Calif.

PARADOXICAL SYMPTOMS IN RIGHT TEMPORAL LOBE TUMOR. LEO STONE, J. Nerv. & Ment. Dis. **79**: 1 (Jan.) 1934.

Stone describes the case of a man, aged 52, with a spongioblastoma multiforme involving the hippocampal gyrus, the corpus striatum and the uncinate portion of the right temporal lobe; anteriorly the growth impinged on the frontal lobe in the olfactory region; posteriorly it extended to the pons posterior to the point where it became continuous with the cerebral peduncles. The author comments on certain features of the case which are paradoxical. Thirty years previously the patient had a nervous breakdown during which he complained of similar symptoms. Was there something at that time which may have later developed into the tumor of the brain? The occurrence of homolateral visual hallucinations in case of tumor of the temporal lobe in the presence of a contralateral defect of the visual field is of interest because in the classic concept the hallucinations occur in the eye with the defective field. The patient was right-handed and yet had aphasia from a lesion on the left side. A dense superficial shadow of the frontal lobe was seen in the roentgenogram in this case, but nothing was found to account for it.

Persistent joking with the preservation of personal physical dignity and a grave and unusual concern over his situation constituted another paradox in the patient. Distinct diminution of the sense of smell homolaterally is unusual in the case of a tumor with hardly demonstrable involvement of the frontal lobe. As a surprising number of persons with psychoneurotic complaints may be found to have tumor of the brain, the author assumes that nervous complaints have an important organic basis even when psychologic motivation seems certain.

HART, Greenwich, Conn.

TREATMENT OF NEUROSYPHILIS WITH ACETARSONE GIVEN INTRAVENOUSLY. LEO SPIEGEL, Am. J. Syph. & Neurol. **18**: 56 (Jan.) 1934.

Acetarsone is a compound containing 27 per cent arsenic in pentavalent form. Chemically it is the sodium salt of 3 acetyl-amino, 4 hydroxy-phenyl-arsonic acid. Spiegel reports on its intravenous use in twenty-five cases of neurosyphilis over a period of seventeen months. The preparation used was made by dissolving 1 Gm. of acetarsone in 9 cc. of a normal solution of sodium hydroxide and then adding 11 cc. of distilled water to the solution. After filtering it was administered intravenously by syringe. Untoward reactions were few and mild, and no ocular disturbances were noted. Of the nine patients with tabes in the group, seven showed definite clinical improvement. Of six patients with meningovascular syphilis, the Wassermann reaction was reduced from positive to negative in two and from strongly to weakly positive in four. One patient with dementia paralytica who was treated with acetarsone showed definite clinical improvement. Seven of the subjects had asymptomatic neurosyphilis. Improvement was therefore measured by serologic response. Of these seven, two had and retained negative Wassermann reactions of the spinal fluid; one showed a reduction from a strongly to a weakly positive reaction, and the other four exhibited a change from a positive to a doubtful or negative reaction. In all cases the cell count was reduced.

Although reluctant to draw conclusions from so small a number of cases, Spiegel thinks that this experience justifies an opinon that acetarsone is a safe, efficient and rapid method of producing good results in the treatment of neurosyphilis.

DAVIDSON, Newark, N. J.

MENTAL DISORDERS RELATED TO CHILDBIRTH. GEORGE FRUMKES, J. Nerv. & Ment. Dis. **79:** 540 (May) 1934.

Mental disorders which follow pregnancy and childbirth are not specific entities but should be classified like other mental disorders. Seven cases in which the psychoses were either precipitated or aggravated by pregnancy or childbirth are cited. Two of these were cases of manic-depressive psychoses of the manic type; four were cases of dementia praecox, two being of the paranoid type and two of the catatonic type, and one was a case of psychoneurosis of the psychasthenic type. In four the psychosis which developed directly after childbirth was the first attack; in two pregnancy occurred during the course of a mental disorder but aggravated the condition, and in one it precipitated a new attack of manic-depressive psychosis.

Care should be taken not to include in the group of psychoses with other somatic diseases those which belong in other groups. A psychosis is often so classified because the patient had a severe labor, had a minor infection or gave wrong answers to questions testing the sensorium at the period when the psychosis was first noticed. These disorders present interesting psychologic problems, some of which are briefly discussed. A relatively frequent symptom is the development of a delusion that the baby is dead. Three of the author's patients had this delusion.

Frumkes emphasizes that pregnancy, lactation and childbirth call for psychologic as well as physiologic adjustment; for example, the patients with an unfavorable psychologic make-up may have the delusion that the child is dead as a means of denying childbirth. Some even deny marriage itself.

HART, Greenwich, Conn.

RETROBULBAR NEURITIS—SINUSITIS—MULTIPLE SCLEROSIS. G. WEILL and J. NORDMANN, Rev. d'oto-neuro-opht. **12:**496 (July-Aug.) 1934.

Among the medical problems solution of which depends on the collaboration of neurologists, ophthalmologists and rhinologists is the problem of acute retrobulbar neuritis. A large number of patients who recover spontaneously later are found to have multiple sclerosis. An increasing number of patients with bilateral subacute retrobulbar neuritis (atypical cases) have later manifested multiple sclerosis in spite of early operation on the posterior sinuses.

Two cases are reported, in both of which multiple sclerosis became manifest three and six years, respectively, after apparent recovery. Both patients had suppurating sinuses which were operated on. Atypical retrobulbar neuritis is attributable in general to disease of the chiasmal region or of the posterior sinuses. Behr produced in rabbits signs of multiple sclerosis by transplanting mucosa from the sinuses into the cranial cavity. At least in some cases of multiple sclerosis and retrobulbar neuritis, the bucconasal route of infection must be assumed. "Interventionists" should review their old case histories to determine the number in which multiple sclerosis has developed and compare their findings with the statistics in cases in which operation was not performed. If the incidence of multiple sclerosis in such cases is really rarer after curettage of the sinuses, Weill and Nordmann will join the ranks of interventionists in order to try to prevent the onset of multiple sclerosis. Spontaneous recovery nearly always takes place in cases of retrobulbar neuritis.

DENNIS, San Diego, Calif.

A GROWTH DEFICIENCY CURABLE BY WHEAT GERM OIL. HAROLD BLUMBERG J. Biol. Chem. **108:***227* (Jan.) 1935.

Blumberg describes the preparation of a highly purified diet by obtaining the protein, carbohydrate, salts and yeast of the basal ration in a fat-free state and then supplementing them with sources of the fat-soluble vitamin A and D and the essential unsaturated fatty acid (vitamin F) in a practically pure form. Such a diet failed to promote normal growth in the rat in the early and middle periods; prolonged feeding (from forty to fifty weeks) to female rats produced a deficiency disease marked by a significant loss of weight, loss of vigor, emaciation, muscular

disturbance and a general lack of well-being. In this poor nutritive state the females sometimes showed a disturbance in the estrous cycle, with consequent cessation of ovulation. The condition was readily curable by certain foods, notably wheat germ, wheat germ oil and egg yolk, the addition of any one of which soon restored growth and well-being.

The preparation of active concentrates by extraction with ether and other fat solvents indicated the vitamin-like nature of the beneficial factor. In distribution and general properties the growth principle resembled vitamin E.

From production of the deficiency and its cure by wheat germ oil and by other substances, Blumberg concludes (*a*) that vitamin E is necessary not only for reproduction and late growth stimulation but also for normal growth in the early and middle periods and for the maintenance of well-being or (*b*) that wheat germ oil contains an unrecognized fat-soluble growth factor. Some evidence favors the latter view.

IRVINE, Boston.

METHOD OF OBTAINING EXACT MEASUREMENTS OF THE SPINAL FLUID PRESSURE. K. HAUG, Monatschr. f. Psychiat. u. Neurol. **86**:355 (Sept.) 1933.

By making continuous measurements of the spinal fluid pressure over prolonged periods of time, Haug found that if certain precautions were used more accurate measurements could be obtained by the customary method of procedure. In general, the tests should not be performed earlier than on the day following the patient's admission, for affective disturbances associated with arrival at the hospital may influence the results. All medication should be avoided if possible. Alcohol, amyl nitrite, histamine, calcium and caffeine are especially apt to change the readings. While it is not absolutely essential for the patient to be in a fasting condition, the stomach should not be overloaded. A full bladder or bowel may raise the spinal fluid pressure considerably. The readings must be made with the patient in a horizontal position. If necessary, the needle may be inserted with the subject in a sitting position, but the patient must then be placed horizontally. Before any readings are made, the patient should assume a comfortable posture with the head resting on a small pillow in its natural position in relation to the thorax and with the lower extremities moderately flexed but not pressing against the abdomen. The patient must be kept warm. The pressure should be read only after it has reached a stationary level. In some cases it is necessary to wait ten minutes before this occurs. However, it was found that a stationary level could usually be obtained within one minute if the patient breathed deeply through the open mouth three or four times and then resumed normal breathing.

ROTHSCHILD, Foxborough, Mass.

SPINAL TERMINATIONS OF THE PROJECTION FIBRES FROM THE MOTOR CORTEX OF PRIMATES. E. C. HOFF and H. E. HOFF, Brain **57**:454 (Dec.) 1934.

A review of the literature discloses a rather wide diversity of evidence concerning the final terminations of the pyramidal fibers, largely attributable to the limitation of the methods used in tracing degenerating fibers. E. C. and H. E. Hoff applied the method based on degeneration of the *boutons terminaux* following the extirpation of the excitable cortex of monkeys and one chimpanzee. They found that following unilateral extirpation of the motor cortex (area 4 of Brodmann) alone, degenerated nerve fiber endings were found in the cervical and lumbar enlargements on dendrites and cell bodies lying in the intermediate zone of the contralateral gray matter and in the ventral horn. Fewer degenerated *boutons*, were similarly distributed on the ipsilateral side. In the thoracic segments degeneration of *boutons* could be demonstrated on both sides of the cord, chiefly around cells lying ventral and lateral to Clarke's column. Removal of the motor area after complete degeneration of pyramidal fibers from the premotor area (area 6 of Brodmann) resulted in degeneration restricted mainly to cells in the mid-region of the gray matter on the contralateral side. Only a few degenerated *boutons* were present in the ventral horn or on the ispsilateral side. When both

the motor and the premotor area were removed at one operation, degeneration of *boutons* occurred mainly around cells in the midregion and at the base of the dorsal and ventral horns of the contralateral sides, but it was also noted on cells evenly distributed throughout the entire ventral horn of both sides. Some degenerated nerve endings were found on motor neurons. SALL, Philadelphia.

HYPERTENSIVE MENINGITIS OF RHINOLOGISTS AND SEROUS MENINGITIS AND ARACHNOIDITIS OF NEUROLOGISTS. J. RAMADIER, Rev. d'oto-neuro-opht. **12**:491 (July-Aug.) 1934.

Ramadier questions the identity of the pathologic processes in cases of serous meningitis, familiar to neurologists, and in cases of otogenous hypertensive meningitis. While otogenous meningeal hydrops presents itself as an episodic physiologic disturbance, of sudden onset but of brief duration, and most often as a single attack, the serous meningitis of neurologists appears as a meningeal, or more probably as an encephalomeningeal condition, slowly progressive and subject to evolutive exacerbations. Again, in comparing the cystic arachnoiditis of neurosurgeons with the endocranial syndrome observed by otologists, at times accompanying an otitis or following a radical operation on the mastoid, differences are observed. In the latter process the phenomena appear more or less rapidly, with signs referable to the cerebellum or the labyrinth, and when the dura is incised cerebrospinal fluid spurts out and the patient is miraculously cured. On the contrary, posterior cystic arachnoiditis often presents a perfect picture of tumor of the cerebellopontile angle; an extensive operation (as for tumor) is required, and adhesions must be broken. The process is prone to return as a result of the formation of new adhesions.

The clinical report of Moulonguet and Anglade, "Hypertensive Syndrome of the Posterior Cerebellar Fossa Mistaken for Cerebellar Abscess" *(Rev. d'oto-neuro-opht.* **12**:513, 1934), presents a perfect example of otogenous meningeal hydrops.

DENNIS, San Diego, Calif.

CEREBRAL ANGIOGRAPHY. EGAS MONIZ, Lancet **2**:1144 (Nov. 18) 1933.

Cerebral angiograms are obtained by means of an injection of from 10 to 16 cc. of thorium dioxide into the inferior part of the common carotid artery between the two portions of the sternocleidomastoid muscle. An arteriogram may be produced if a roentgenogram is taken one second after injection. Another roentgenogram obtained after an interval of four seconds will show the veins and the sinuses of the brain. These two sets of roentgenograms are taken following the same injection. The patients have little inconvenience and are able to leave the hospital immediately after the roentgenograms are obtained. Moniz claims that this method is of great value in the diagnosis and localization of cerebral neoplasms. Of importance is the disturbance of one of the following arterial formations: (1) the bend of the internal carotid artery as it transverses the cavernous sinus, the so-called carotid syphon; (2) the sylvian group, which is composed of the middle cerebral artery and its branches, and (3) the anterior cerebral artery and its branch, the pericallosal artery. A tumor either displaces or distorts these constellations, depending on their localization. Abnormal or increased vascularity of tumors can readily be seen. A knowledge of the main arterial supply of such a neoplasm may be of great aid to the surgeon. Aneurysms may be demonstrated. Seven roentgenograms are shown, including two normal arteriograms and one phlebogram.

BECK, Buffalo.

PAPILLARY STASIS AND RETINAL ARTERIAL HYPERTENSION WITHOUT HYPERTENSION OF THE CEREBROSPINAL FLUID, IN THE COURSE OF A LOW GRADE OTITIC MENINGITIS: THE MECHANISM OF PAPILLARY STASIS. H. TILLÉ, Rev. d'oto-neuro-opht. **12**: 336 (May) 1934.

Following an old complicated suppurative otitis on the left side, there developed diffuse meningitis of the left convexity. The evolution was clinically and cytologically favorable up to the twenty-seventh day after an operation on

the mastoid. Hypertension of the central artery of the retina and slight papillary stasis preceded the fatal outcome by nine days, as the sole alarming symptoms (there was slight hypotension of the cerebrospinal fluid). According to some writers, hypertension of the cerebrospinal fluid conditions, by reflex adaptation, retinal arterial hypertension. Study of the graphs in this case shows that retinal arterial hypertension may also reveal a preceding vascular state which is capable of causing hypertension of the cerebrospinal fluid, or it may remain isolated. The earliest phenomenon, then, that can be made clinically evident is not hypertension of the cerebrospinal fluid, as is assumed in all modern theories of papillary stasis, but the vascular disturbance, one element of which this study has demonstrated. This fact does not diminish the semeiologic value of retinal hypertension; it remains a sign of intracranial hypertension, but both it and papillary stasis may precede the intracranial hypertension. DENNIS, San Diego, Calif.

ARTERIOSCLEROSIS OF THE LUMBAR SEGMENTAL ARTERIES PRODUCING ISCHEMIA OF THE SPINAL CORD AND CONSEQUENT CLAUDICATION OF THE THIGHS: A CLINICAL SYNDROME WITH EXPERIMENTAL CONFIRMATION. FREDERICK LEET REICHERT, DAVID A. RYTAND and EDWIN L. BRUCK, Am. J. M. Sc. **187**:794 (June) 1934.

Some of the literature in regard to intermittent claudication of local vascular origin, paraplegia due to ischemia of the extremities or of the spinal cord and intermittent paraplegia (due to caisson disease and malaria) is reviewed. In dogs in which ligation of the lower abdominal part of the aorta or ligation bilaterally of one or more lumbar segmental arteries was performed, weakness of the hind-limbs, accompanied at times by temporary incontinence and associated with a delayed spasticity, occurred. Four patients who had a nonsyphilitic arteriosclerosis exhibited a spastic gait without positive neurologic signs, and weakness of thighs and hips (intermittent claudication). All the roentgenograms revealed calcification in the lower abdominal part of the aorta. The condition in these patients was attributed to ischemia of the spinal cord produced by alterations in spinal branches of the arteriosclerotic lumbar segmental arteries. MICHAELS, Boston.

RECURRENT POLYNEURITIS IN PREGNANCY AND THE PUERPERIUM AFFECTING THREE MEMBERS OF A FAMILY. C. C. UNGLEY, J. Neurol. & Psychopath. **14**:15 (July) 1933.

A mother and two daughters were affected with a recurrent polyneuritic syndrome at different times during a period of twenty years, which was related to childbirth. Severe pains, usually radiating from the scapula down into the arm, set in and were followed by the rapid onset of flaccid paralysis in the muscles of the same limb. Extension of the paralysis was usually accompanied by further pains during the next few months. Sensory impairment and wasting generally occurred and, despite the general recovery in the ensuing twelve to eighteen months, sometimes persisted. The paralysis was asymmetrical and frequently widespread but was confined to the upper extremities. The sensory and motor disturbance could not be correlated with the distribution of peripheral nerves or spinal segments. Laboratory and other investigations for etiologic factors gave negative results. There was no evidence of syphilis or of other infections, of the toxemia of pregnancy, of vitamin deficiency, of poisoning from lead, alcohol or hematoporphyrin, of cervical ribs or of hypertrophic nodules.

SPERLING, Philadelphia.

POST-INFLUENZAL RECOVERY FROM DEPRESSION. MAX LEVIN, Am. J. Psychiat. **13**:345 (Sept.) 1933.

Recovery from psychotic depression following an attack of influenza has been previously reported in only two cases. To these Levin adds a third case. His patient had an attack of depression in 1918 (then at the age of 28) following

premature labor. She was slow, apathetic and depressed and lost weight and appetite during the depression. In the tenth month of the depression she contracted influenza. The symptoms, which were mild, consisted of fever, headache and generalized pains and aches. There was no somnolence, delirium, diplopia or other evidence of encephalitis. On the fourth day of the illness she felt well enough to get up; at that precise moment the family noticed that the depression had disappeared. She looked and felt normal; she recovered her lost weight and appetite and in every respect behaved like a normal woman for twelve years thereafter. In 1930 she had a second attack of depression with many paranoid trends, from which, at the time of writing (January 1933), she had not recovered.

DAVIDSON, Newark, N. J.

ACROPARESTHESIA AND QUINIDINE. SMITH ELY JELLIFFÉ, J. Nerv. & Ment. Dis. **79:** 631 (June) 1934.

Jelliffe describes a series of attacks of acroparesthesia starting with mild paresthetic disturbances and becoming more painful with the use of larger doses of quinidine. When the drug was discontinued the sensory symptoms disappeared. Factors to be considered as possibly causative are: (1) modification of metabolism due to quinidine, (2) modification of the tonicity of the musculature of the peripheral blood vessels due to the same cause, (3) action on receptors of sensory systems by the toxic agent, (4) age, (5) arthritic tendencies, (6) arteriosclerotic tendencies, (7) attacks of auricular fibrillation indicative of modification in the response of the cardiac-neuromuscular apparatus, (8) special biochemical spasmophilic tendencies and (9) personality factors.

For the most part the literature on quinine and quinidine is silent on the subject of acroparesthesia. The drug in the author's case may have been a precipitating or a convergent factor. Senescent arthritic changes often accompany this symptom. Jelliffe dilates on the possible relationship to Paget's disease and calcium metabolism in his inimitable humorous fashion.

HART, Greenwich, Conn.

GRAVE MYOPIA AND NANISM FROM HEREDITARY THYROHYPOPHYSEAL DYSMORPHOSIS AND CRANIAL AND FACIAL DYSOSTOSIS. E. AUBARET and G. E. JAYLE, Rev. d'oto-neuro-opht. **12:**561 (Sept.) 1934.

The inspiration for this article is the study of a woman, aged 48, with myopia, exophthalmos, nanism and craniofacial dysostosis. The hereditary influence is shown by two paternal aunts, the grandmother and a distant cousin, who had a small figure like that of the patient but did not have exophthalmos. Involvement of the vegetative system was shown by excessive sweating and a positive oculocardiac reflex. Laboratory tests gave negative reactions except for showing dysfunction of the anterior lobe of the hypophysis and of the thyroid and ovary. A roentgenographic study revealed marked prognathism of the superior and inferior maxillas, hyperdevelopment of the craniofacial sinuses, disproportion between the volume of the skull and the volume of the face, diminution of the depth of the orbits and a tendency of the floor of the ethmoid sinus to incline toward the vertical plane. The thyrohypophyseal factor was indicated by disturbance of the hairy development, a suggestion of the sign of the eyebrow of Leopold Levi, disturbance of osseous development, the state of the skin and infantilism. The condition belongs to the group classified as oxycephaly and Crouzon's disease.

DENNIS, San Diego, Calif.

SEGMENTAL DAMAGE TO THE SPINAL CORD FOLLOWING INJURY TO THE PERIPHERAL NERVE. NIESSL VON MAYENDORF, Monatschr. f. Psychiat. u. Neurol. **85:**243 (May) 1933.

Niessl von Mayendorf reports the case of a woman, aged 35, who sustained a lacerated wound of the left hand. Infection set in, and healing did not occur for several months. Three years later weakness of the right hand with loss of

sensation was noted. Examination in the following year disclosed atrophy of some muscles of the right shoulder with loss of power and atrophy of the extensor muscles of the right arm. The muscles of the right forearm and the small muscles of both hands showed slight wasting. There were analgesia of the skin of the right upper extremity and hypalgesia of the skin of the left upper extremity. The right hand and arm showed impairment of temperature sensation. According to the author this case corroborates the view that severe injuries to the hand with resulting infection may lead to syringomyelia-like changes in the spinal cord. Apparently toxins formed in the wound gain entrance to the spinal cord by spreading up the nerve sheaths. Experimental observations and cases recorded in the literature which support these views are mentioned.

ROTHSCHILD, Foxborough, Mass.

THE PROPRIETY OF DIAGNOSTIC LUMBAR PUNCTURE IN INTRACRANIAL HYPERTENSION. W. F. SCHALLER, J. Neurol. & Psychopath. **14**:116 (Oct.) 1933.

The author contends that there is no evidence that foraminal herniation follows spinal puncture with open craniospinal pathways, even in the presence of increased intracranial pressure due to a sudden wedging of the contents of the posterior fossa into the foramen magnum. This so-called herniation may occur in general swelling of the brain and edema and may arise from changes in intracranial pressure and vasomotor paralysis, which may be produced by sudden and excessive removal of spinal fluid. Supporting this contention is the greater incidence of postpuncture accidents in cases of supratentorial than in those of infratentorial tumors, and the greatest incidence in cases of vascular lesions. Experimental studies of the fluid and movement of the structures of the brain in cadavers in which lumbar and cisternal drainages were performed under varying pressures in different portions of the cerebrospinal fluid pathways produced no evidence of movement of the structures in the posterior fossa or of interference with the cerebrospinal fluid pathways, except on distortion of a cerebellar lobe. In dogs with increased intracranial pressure the rapid and excessive removal of fluid produced subsequent cerebral edema.

SPERLING, Philadelphia.

DELIRIOUS AND DREAMLIKE CONFUSED STATES IN MANIC-DEPRESSIVE DISORDERS (A CONTRIBUTION TO THE QUESTION OF THE EXTENT OF THE SYMPTOMS OCCURRING IN THE MANIC-DEPRESSIVE SPHERE). E. ILLING, Monatschr. f. Psychiat. u. Neurol. **85**:366 (May) 1933.

Illing reports three cases of manic-depressive psychosis in which episodic delirious and confused states occurred. They were characterized by a dreamlike clouding of consciousness with many fantastic ideas and plastic, rapidly changing hallucinations. Illing was unable to find any exogenous factors to account for the episodes. There was no evidence of unusual constitutional factors pointing to a schizophrenic element in the psychoses. In one case he was able to corroborate the observation of Mayer-Gross and Rehm that a strong imagination, lively fantasies and plastic dreams were features of the prepsychotic personalities of manic-depressive patients showing these episodes. The conclusion is drawn that the disease concept manic-depressive psychosis may include, in addition to manic and melancholic syndromes, other clinical features without thereby leading one to question the diagnosis and to presuppose that complications have occurred.

ROTHSCHILD, Foxborough, Mass.

OTITIC HYDROCEPHALUS. HUGH G. GARLAND, Lancet **2**:751 (Sept. 30) 1933.

The intracranial complications of otitis media comprise many clinical and pathologic conditions; among them is a well defined syndrome for which the name otitic hydrocephalus was first suggested by Symonds in 1931. This syndrome can usually be diagnosed on the basis of clinical manifestations, and it responds

rather dramatically at time to simple therapeutic measures. The clinical manifestations of otitic hydrocephalus are: its occurrence is almost entirely confined to children and young adults, complicating either acute or chronic otitis media; headache is frequent and may be either severe or slight; papilledema is constant, although vomiting and nausea are variable; the mental reaction is usually undisturbed, but dulness has been present in a few instances in which there has been a high grade of papilledema; the cerebrospinal fluid is under high pressure and of large volume but is normal chemically and bacteriologically. The condition usually clears up after weeks or months as a result of repeated lumbar puncture. If this procedure is not frequently carried out optic atrophy may ensue.

BECK, Buffalo.

SOME ALARMING SEIZURES. JOHN A. RYLE, Brit. M. J. **1**:89 (Jan. 20) 1934.

Ryle discusses in considerable detail "seizures" or "nerve storms," such as migraine, vertigo and the vasovagal attacks of Gowers. A concise description is given of the symptomatology in each of these conditions, and there are illustrative case reports. Several features are common to these conditions, which are classified as paroxysmal neuroses. They tend to occur in persons of particular types of temperament; they are paroxysmal, intermittent and of limited duration and are associated with, and leave in their train, no structural nervous or visceral damage. They tend to create grave anxiety and apprehension and are more likely to develop at times of general unfitness, whether physical or mental. They seem to merge with one another and to possess common clinical features and etiologic characters. The vasomotor phenomena of fainting, namely, coldness and pallor, are common to all three conditions, and in all three loss of consciousness may occasionally occur. In regard to treatment, it is essential to examine carefully, to explain simply and to reassure fully so as to remove, so far as possible, the crippling element of doubt and fear.

FERGUSON, Niagara Falls, N. Y.

PSYCHOSES WITH DIABETES. O. JANOTA and J. STŘÍTESKÝ, Monatschr. f. Psychiat. u. Neurol. **83**:17 (June) 1932.

Apart from mental disturbances associated with coma, psychoses of an exogenous nature rarely occur in cases of diabetes. The authors report a case of this type in a woman aged 34. The patient had shown symptoms of diabetes for several months, following which there developed a psychosis resembling an amentia. The chief features were defective grasp of the surroundings, mistaking of persons, incoherence, excitement, perplexity and emotional outbursts. The sugar content of the blood was 267 mg. per hundred cubic centimeters. The urine showed from 7 to 8.5 per cent of sugar and a large amount of acetone. The patient was given insulin and a diet relatively high in carbohydrate. Although the diabetic condition improved rapidly, the psychosis continued, assuming a paranoid and depressive trend. The mental symptoms disappeared completely within three and one-half months. They recurred several months later when treatment was neglected but disappeared promptly when treatment was resumed.

ROTHSCHILD, Foxborough, Mass.

TUBEROUS SCLEROSIS WITH EPILEPSY (EPILOIA) IN IDENTICAL TWINS. HOWARD FABING, Brain **57**:227 (Oct.) 1934.

Fabing reports tuberous sclerosis with epilepsy in identical twin girls. This is the first published report of this nature appearing in the literature. He bases his diagnosis on the presence of epileptiform seizures and mental impairment and the presence of varied cutaneous lesions such as vascular nevi of the capillary type, small pigmented raised nevi, anemic nevi of Vorner, fibroma molluscum and cutaneous lesions of the face which he considers to be true adenoma sebaceum. One of the patients presented a cardiac irregularity and anomalies of the right kidney. Fabing offers the possibility that these may be due to cardiac rhabdomyoma and

tumor of the primordial primitive kidney, conditions which have been reported in association with tuberous sclerosis. The cutaneous lesions of the twins were mirror images of one another, and the author speculates on the possibility of genotypical heredity versus blastophoric injury in the production of tuberous sclerosis.

SALL, Philadelphia.

CASES OF AURAL VERTIGO AMENABLE TO TREATMENT BY OSSICULECTOMY. JAMES DUNDAS-GRANT, Lancet **2**:1029 (Nov. 4) 1933.

According to Dundas-Grant, certain cases of aural vertigo are suitable for ossiculectomy. Vertigo, either constant or in attacks, headache, convulsions and loss of, or diminished, hearing acuity were among the symptoms which the patients presented. In all cases one or both of two conditions were present: Either the ossicles obstructed the outlet of the attic and so prevented the escape of thickening discharges, or the ossicles were fixed, leading to an immobility of the otherwise mobile stapes. Thus, in the former condition the removal of the ossicles permitted the free escape of the contents of the attic with relief from headache and vertigo and to some extent from dulness of hearing. In the latter condition the restored mobility of the stapes provided the normal safety-valve for variations of intralabyrinthine tension, with disappearance of the vertigo. Ten of the patients who were operated on were entirely cured, and the other two were much relieved of their symptoms.

BECK, Buffalo.

ACETYLCHOLINE HYDROCHLORIDE USED IN THE TREATMENT OF AMAUROSIS DUE TO QUININE, RESULTING IN IMPROVEMENT OF THE VISUAL FIELD. HARTMANN and VOISIN, Ann. d'ocul. **171**:435 (May) 1934.

Hartmann and Voisin report the case of a young man whose vision, after taking 5 Gm. of quinine, was reduced to 1/20, and the visual field was contracted to the macular area. The retina was pale, and the arteries were contracted. On the following day six injections of 120 cg. of acetylcholine hydrochloride were administered. After the first injection vision improved. The same amount of acetylcholine hydrochloride was given for eight days, with constant improvement in vision and enlargement of the visual field, especially on the temporal side. On the ninth day, 40 cg. of acetylcholine hydrochloride was administered. The visual field improved to 20 degrees nasally and 50 degrees temporally.

BERENS, New York.

COMA DUE TO A BARBITURIC PREPARATION FOLLOWED BY TRANSIENT XANTHOPIA. J. EUZIERE, J. VIDAL, H. VIALLEFONT and J. M. BERT, Rev. d'oto-neuro-opht. **12**: 344 (May) 1934.

Many facts show that the perception of colors has not exclusively a peripheral substratum, for example, the case of Wechsler in which there was dissociation between cortical vision and color vision. Such cases are evidently caused by encephalic and not by retinal lesions. In the toxemias, disturbances of color vision vary with the poison. Following the ingestion of a large amount of a barbituric preparation, a patient was comatose for several hours. When consciousness returned, objects appeared to have a yellowish color. This phenomenon persisted for three or four days. It is suggested that there was an elective inhibition of color perception, permitting only the conception of the idea of yellow.

DENNIS, San Diego, Calif.

INCREASED INTRAOCULAR TENSION IN YOUNG PERSONS AS A CAUSE OF SEVERE FRONTAL HEADACHE. R. L. RAYMOND, Brit. M. J. **1**:102 (Jan. 20) 1934.

Four cases are described in the belief that they may represent a symptom complex that is not commonly recognized. Each of the patients complained of frontotemporal headache of varying degree and radiation; each was a man between

20 and 30 years of age—before the typical age for the development of glaucoma. In each case the pain was increased by pressure on the eyeball, and the tension of the eyeball, as estimated by digital examination, was thought to be higher than in the other eye. No other physical findings were observed to account for the symptom complex. Raymond thinks that many frontal headaches that are diagnosed as migraine in the absence of vomiting and nausea may be due to increased intra-ocular tension.

FERGUSON, Niagara Falls, N. Y.

ECONOMIC STATUS AS A FACTOR IN JUVENILE DELINQUENCY. T. EARL SULLENGER, J. Juvenile Research **18**:233 (Oct.) 1934.

The relationship of delinquency to physical health in 225 families in Omaha which were receiving public aid was tabulated. The number and types of agencies with which 500 families were registered, the number of rooms in the homes of 100 children committed to institutions because of delinquency, their ages and intelligence quotients, the types of homes with the percentage of successes and failures in checking delinquency, the proportion of successes to failures and a comparison with the conditions of homes in Omaha with those in other cities were included in this survey. The author concludes that poverty is less important than defective family relationships but that elimination of the former will nevertheless aid greatly in the problem of delinquency.

ALLEN, Philadelphia.

A CASE OF SIMMONDS' DISEASE. LÉANDRE CERVERA, ALBERT FOLCH and BONAVENTURA BENAIGES, Rev. franç. d'endocrinol. **12**:15 (Feb.) 1934.

The authors report increase in weight and general improvement in the case of a girl, aged 15 years, suffering from Simmonds' disease. The treatment consisted of the application of high voltage roentgen rays to the temporal, occipital and superior parietal regions. The focal distance was 40 cm.; the filter used was 0.005 zinc and 0.002 aluminum; the tension was 120 kilowatts, and the daily dose 150 roentgens. The treatments were given every other day, and the field was regularly changed in order to avoid loss of hair. In addition, the patient was given an extract of the anterior lobe of the pituitary and vitamin therapy.

NOTKIN, Poughkeepsie, N. Y.

ENDOBUCCAL AND PERIBUCCAL DISTURBANCES FOLLOWING RETROGASSERIAN NEUROTOMY. PAUL ACHARD, Rev. d'oto-neuro-opht. **12**:507 (July-Aug.) 1934.

Functional disturbances of the masticator apparatus following retrogasserian neurotomy have been overshadowed by the more important complication of the loss of the eye on the side of the operation. These disturbances consist of complete suppression of the gingivogenal sensation and paralysis of the masticator muscles, accumulation of food in the mouth, ulceration of the cheeks and deviation of the mandible, accompanied by malocclusion. Since these patients are usually toothless, a properly devised prosthesis will obviate the ulcerations and furnish better occlusion of the artificial teeth.

DENNIS, San Diego, Calif.

PROGRESSIVE PARALYSIS OF THE NERVUS INTEROSSEUS DORSALIS. HENRY W. WOLTMAN and JAMES R. LEARMONTH, Brain **57**:25 (March) 1934.

Cases of isolated paralysis of the nervus interosseus dorsalis are not common. Five cases are presented; in one the affected nerve was explored, the only apparent explanation being an anatomic peculiarity of the course of the nerve. In all the cases the paralysis was progressive, beginning with weakness of the extensor muscles of the fifth finger and extending radially to involve both superficial and deep branches of the nerve. The normal and anomalous course of the nerve is described.

MICHAELS, Boston.

PERONEAL MUSCULAR ATROPHY IN FIVE GENERATIONS. JAN GORDON, Lancet **2**:1026 (Nov. 4) 1933.

A family tree is presented covering five generations in which there were thirteen persons with peroneal muscular atrophy of the Charcot-Marie-Tooth type. Heredity is important but not constant in this disease. This group of cases, however, is noteworthy, not only because there was a family history but also because it could be established that transmission occurred only through affected females. Male and female progeny were affected. Two case histories are included.

BECK, Buffalo.

SYNDROME OF ENCEPHALITIS, FOLLOWED BY A HYPOPHYSEAL SYNDROME. CARLOTTI, JACQUET and DESREMAUX, Rev. d'oto-neuro-opht. **12**: 340 (May) 1934.

The patient, a woman aged 30, suffered from a typical attack of encephalitis in August 1932. Visual disturbances appeared in the following February and were soon accompanied by obesity, cessation of menstruation, enlargement of the hands and feet, papillary stasis and narrowing of the visual fields. A roentgenogram revealed enlargement of the sella turcica. The chiasmal syndrome was not present. No similar case is known to the authors.

DENNIS, San Diego, Calif.

CHARACTERISTICS OF PROBLEM CHILDREN. PAUL L. BOYNTON and BONNIE H. MCGAW, J. Juvenile Research **18**:215 (Oct.) 1934.

Boynton and McGaw state there has been much discussion of problem children in school but little delineation of characteristics that cause teachers to so brand the children. Sixty-six teachers of the fifth grade in the public schools of Nashville, Tenn., were given questionnaires, and the answers were tabulated. It was concluded that, to the teacher, a problem child is chiefly one who interferes with school discipline; consequently teachers should have some training in recognition of more fundamental disturbances.

ALLEN, Philadelphia.

THE CLINICAL RECOGNITION OF STRUCTURAL DISEASE OF THE PERIPHERAL VESSELS. GEORGE W. PICKERING, Brit. M. J. **2**:1106 (Dec. 16) 1933.

Impairment of the circulation in a limb may result in two ways: from structural disease of the vessels with consequent permanent reduction in their caliber or from excessive narrowing (spasm) of vessels that are yet able to expand widely. Pickering discusses in considerable detail methods of determining the various causes of impairment of circulation in the extremities, of making differential diagnoses and of determining procedures for treatment. The nature of the article is such that an abstract would be inadequate.

FERGUSON, Niagara Falls, N. Y.

ANGIONEUROTIC OEDEMA. WILLIAM LENNON, Lancet **2**:729 (Sept. 30) 1933.

A useful summary of the chief features of angioneurotic edema is given, based on the observation of ten patients. Almost invariably there is either a family history or a personal history of some allergic disease. When the condition is allergic, the patient himself frequently is cognizant of the offending drug or food. In an acute attack, epinephrine is the most useful drug. However, a combination of epinephrine and solution of pituitary is of especial value in controlling swelling of the mouth and may ward off the possibility of a tracheotomy if the larynx is involved.

BECK, Buffalo.

THE EMOTIONAL STABILITY OF TEACHERS AND PUPILS. PAUL L. BOYNTON, HARRIET DUGGER and MASAL TURNER, J. Juvenile Research **18**:223 (Oct.) 1934.

In an attempt to increase knowledge of the relationship of emotional stability of teacher and pupil the introspective method was employed. Questionnaires

were given to 73 teachers and 1,095 students. Signatures were not required. The results were graded and tabulated, and the conclusion was reached that emotionally unstable teachers tend to have associated with them unstable children.

ALLEN, Philadelphia.

THE TREATMENT OF PELLAGRA WITH CERTAIN PREPARATIONS OF LIVER. JULIAN M. RUFFIN and DAVID T. SMITH, Am. J. M. Sc. **187**:512 (June) 1934.

Ten patients with active pellagra subsisting on a basic diet deficient in vitamin G (B_2) showed satisfactory remissions after the daily oral administration of 90 cc. of an aqueous extract of liver. No improvement was observed in five patients with pellagra who were treated with solution of liver extract in doses of 5 cc. given intramuscularly.

MICHAELS, Boston.

LIPODYSTROPHIA PROGRESSIVA. W. HARTSTON, Lancet **2**:1916 (Dec. 23) 1933.

Two additional cases of lipodystrophia progressiva, both in boys aged 11 years, are described. From the data supplied by these cases, along with observations made in the eighty-five authentic cases already reported in the literature, a short and careful account of the syndrome is given. The current theories as to etiology are discussed.

BECK, Buffalo.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, Jan. 8, 1935

C. BURNS CRAIG, M.D., *Chairman of the Section, Presiding*

METABOLISM OF CREATINE IN DISEASE OF THE MUSCLES: THE CLINICAL SIGNIFICANCE OF THE EFFECT OF GLYCINE ON THE EXCRETION OF AND ON THE TOLERANCE FOR CREATINE. DR. A. T. MILHORAT (by invitation) and DR. H. G. WOLFF.

The purpose of this investigation was twofold: first, to understand better the factors determining the excretion of creatine and creatinine, and second, to ascertain in what way such studies can extend knowledge of the pathologic processes in disease of muscles. Forty-six patients presenting a wide variety of abnormalities in the function and structure of the muscles were studied. Among these were 17 with progressive muscular dystrophy in all stages, 7 with myasthenia gravis during periods of exacerbation and remission of symptoms, 2 with myotonia congenita, 1 with amyotonia congenita, 2 with dystonia musculorum deformans and 12 with wasting of the muscles secondary to disease of the anterior horn cells or of the peripheral nerves. In the latter group were patients with acute anterior poliomyelitis, chronic progressive anterior poliomyelitis, amyotrophic lateral sclerosis, so-called "neuronitis" with muscular atrophy, peripheral neuritis and peroneal atrophy of the Charcot-Marie type. In addition, several normal subjects were studied. Twenty patients with various types of disease of muscles, from a previous series, furnished data which were used in formulating conclusions. The patients were studied for periods of from a few weeks to six months.

The urine of patients maintained on a creatine-free diet was collected in twenty-four hour samples, and the creatinine, creatine and total nitrogen content were determined daily. The studies were divided into four test periods. During the first period the spontaneous excretion of creatine was estimated; during the second period excretion was ascertained when the patients were given 1.32 Gm. of creatine by mouth following an adequate control period (referred to as the creatine tolerance test); during the third period the excretion was estimated when the patients were given glycine (20 Gm. daily), and during the fourth period it was ascertained when the patients who were receiving glycine were given creatine in addition.

The normal person excretes creatinine in the urine each day in an amount which varies in different persons but is constant for any one person. There appears to be a definite relationship between the amount of creatine eliminated and the total mass and efficiency of the muscles. Large, well developed men have the greatest output of creatinine, while small-muscled men and women have a smaller output. Children excrete the least creatinine. No creatine, or only a minimal amount, is eliminated by men. A slight or moderate excretion of creatine by women is common. Children normally excrete large amounts of creatine. When creatine is administered it is promptly and almost completely excreted in the urine. However, the normal organism is capable of retaining a considerable amount of ingested creatine without effect on the urinary constituents.

Patients with diseases which affect the muscular system commonly have creatinuria even with a creatine-free diet. Accompanying this there is usually a diminution in the amount of creatinine excreted and in the ability of the body to

retain ingested creatine (a low creatine tolerance). In cases of progressive muscular dystrophy large amounts of creatine are often excreted. The level of the excretion of creatine is usually related to the amount of muscle disability, but in some instances the impairment in the tolerance for creatine appears to afford a better index of the diminution in the mass and functional capacity of the muscles. In advanced stages of the disease the tolerance for creatine can be impaired to the extent that all of an ingested dose of creatine is excreted in the urine. The amount of creatinine excreted is diminished and appears to be related to the amount of functioning muscle still remaining.

In such patients the ingestion of glycine is followed by an increase in excretion of and a further decrease in the tolerance for creatine. The glycine appears to act as an amplifier of the defect in the tolerance for creatine and hence is often of use in demonstrating less obvious defects in the metabolism of creatine. Such effects are not to be confused with the results of prolonged ingestion of glycine.

In most cases of myasthenia gravis only a moderate amount of creatine is eliminated, and the tolerance for creatine is only moderately impaired. However, patients with a rapidly progressive type of disease excrete a large amount of creatine and show a more serious defect in the ability to retain ingested creatine. The diminution in the output of creatinine appears to be proportional to the loss in the functional efficiency of the muscles. The defect in the tolerance for creatine can be exaggerated by the ingestion of glycine during an exacerbation of symptoms. Usually glycine has no effect on creatinine if given during the period of remission.

In cases of amyotonia congenita considerable creatine is usually excreted, the tolerance for creatine is low, and the output of creatinine is much diminished. Glycine increases the excretion of creatine and further decreases the tolerance for creatine. In cases of myotonia congenita no abnormality in the metabolism of creatine or creatinine could be demonstrated by the methods employed.

In patients with myotonia atrophica the diminution in the excretion of creatine appears to be proportional to the reduction in the muscle mass. The amount of creatine excreted is much lower than in patients with progressive muscular dystrophy showing a similar amount of muscle disability. In patients with myotonia atrophica extensive wasting of the muscles and considerable disability of important muscle groups can occur with only a slight or moderate excretion of creatine. The tolerance for creatine is only moderately impaired and is unaffected by the ingestion of glycine. Only patients with extreme involvement of the muscles excrete a large amount of creatine. Then the tolerance for creatine is seriously impaired, and the ingestion of glycine is followed by an increase in the excretion of creatine and a further decrease in the ability to retain ingested creatine. In metabolism of creatine and creatinine, patients with myotonia atrophica resemble patients with wasting of the muscles secondary to disease of the nervous system in whom several muscle groups are uninvolved.

In patients with wasting of the muscles associated with disease of the anterior horn cells or of the peripheral nerves, the diminution in the output of creatinine appears to be proportional to the reduction in the muscle mass. The amount of creatine eliminated is smaller than is observed in patients with progressive muscular dystrophy with a similar amount of muscle wasting. Furthermore, the impairment in the tolerance for creatine is less than in patients with progressive muscular dystrophy. Unless the wasting of the muscles is extensive, glycine is without effect on the excretion of or on the tolerance for creatine. However, when the involvement of the muscles is so extensive as to include most of the stated musculature, defects in the metabolism of creatine and creatinine can be observed that resemble those in advanced stages of progressive muscular dystrophy.

The effect of glycine on the metabolism of creatine as shown in the tolerance for creatine is out of all proportion to the effect of comparable amounts of nitrogen from sources other than glycine and creatine. It is postulated that glycine acts as a precursor of creatine. Moreover, the output of and tolerance

for creatine appear to be an expression of the total mass of improperly functioning muscle and not per se an expression of the amount of wasted muscle or an indicator of the primary site of the disease.

DISCUSSION

DR. E. BRAND (by invitation): Neurologists have always been interested in the metabolism of creatine in muscular disease, and as early as 1870 Rosenthal, a Viennese neurologist, first observed that there was a diminished excretion of creatinine in a case of muscular dystrophy. Similar experiments were later carried out by Langer, who found that various muscular diseases differed in the excretion of creatinine; in some cases the excretion was below normal, and in others, normal. A most important contribution, I believe, was made by Levene and Kristeller in 1909 at the Montefiore Hospital. They first determined not only the amount of creatinine but also the amount of creatine in the urine of patients with muscular disease. Except for refinements, many of the findings of later years were mentioned in their paper. Levene and Kristeller established the fact that the excretion of creatine in cases of muscular disease is dependent on the intake of creatine and on the amount of nitrogen catabolized.

Concerning the excretion of creatinine, it is always stated that it is independent of the diet and of the intake of nitrogen. That is only partially true; A. I. Ringer showed years ago that if a normal person for prolonged periods receives a low amount of nitrogen the excretion of creatinine gradually falls to a very low level. The excretion of creatinine is frequently claimed to be an indicator of the muscle mass. This is apparently only partially true, because after amputations the excretion of creatinine does not change materially. There remain many aspects of the metabolism of creatine and creatinine which are not yet understood.

In recent years it has been found that small and sometimes larger amounts of creatine are excreted by normal males; creatine occurs in the urine of the normal male apparently much more frequently than is claimed in the literature; other investigators have substantiated this point.

For several years my colleagues and I have been engaged in an investigation similar to that presented by Drs. Milhorat and Wolff. We have investigated about 25 cases of neuromuscular disease, about 60 cases of muscular dystrophy and about 10 cases of myasthenia gravis. We agree in a general way with Drs. Milhorat and Wolff, though there may be minor deviations of opinion. In regard to metabolic studies in cases of myasthenia gravis, we do not exactly agree with them. We do not find that disturbed metabolism of creatine and the effect of glycine on the tolerance for creatine are characteristic in this disease. I believe that the opinions of Drs. Boothby and Wilder, of the Mayo Clinic, with respect to the metabolism of creatine in cases of myasthenia gravis are similar to ours. We have tested a number of patients with myasthenia gravis along the lines suggested by Dr. Milhorat. In certain cases we found that feeding of glycine had an influence on the tolerance for creatine; in other cases there was no such effect. In two cases we found that glycine had an influence on the tolerance for creatine at one time but no influence at another time. The clinical condition of the patient was about the same for both tests, but the intake of protein was different.

I wish to say something about our present views on the status of glycine therapy in muscular disease, particularly in view of a recent, somewhat misleading editorial in *The Journal of the American Medical Association*. Dr. Harris and I at the New York Psychiatric Institute and Hospital and Zabriskie and Hare at the Neurological Institute of New York treated a fairly large group of patients with muscular dystrophy with glycine for a considerable length of time. Seven have received glycine for from one-half to one year; none have shown any improvement, and a number have become definitely worse. A second group of 20 patients with muscular dystrophy have been receiving glycine for between one and two years; the condition has remained stationary in some, but a considerable number have become definitely worse. A third group of 5 patients with muscular dystrophy have received glycine for between two and

three years; 1 patient has shown questionable improvement, the condition is stationary in 1 with some possible improvement, and 3 patients are definitely worse.

In a recent publication from the Mayo Clinic Dr. Wilder stated that glycine therapy in cases of muscular dystrophy seems to be far from satisfactory. Dr. Boothby said that none of his patients with muscular dystrophy who were receiving glycine therapy had become definitely worse during this period. He further stated that it was his impression that the natural progressive course of the disease had been, at least temporarily, slowed by the glycine therapy. I do not believe, however, that the latter statement can be made at the present time. It is difficult to state that the progress of the disease has been retarded. However, I do not want to say the contrary.

The therapeutic aspects of myasthenia gravis present a picture very different from that of muscular dystrophy. We agree with other observers that glycine may have some therapeutic effect. In the cases studied so far, we are under the impression that ephedrine is more effective. Some patients with myasthenia gravis seem to respond best to treatment with ephedrine plus glycine.

DR. HAROLD G. WOLFF: We have tried to correlate these findings and the clinical facts as they present themselves. The simple formulation that the most serious defect in metabolism of creatine is found in cases of primary myopathy and that a lesser disturbance is found in the metabolism of creatine, in those cases of myopathy secondary to disease of the nervous system did not prove satisfactory, for in patients with extensive wasting the disturbance in the metabolism of creatine may be equally great, whether the wasting is due to primary myopathy or to myopathy resulting from disease of the spinal cord. Then we made an attempt to correlate the findings on the basis of wasting, i. e., the greater the wasting the greater the defect in the metabolism of creatine, but that, too, was unsatisfactory. For example, if one postulates that patients with severe wasting have the greatest disturbance in the metabolism of creatine, one is confronted with the troublesome fact that patients with only mild or moderate degrees of muscle wasting associated with progressive muscular dystrophy show a far greater disturbance in the metabolism of creatine than do patients with very severe wasting secondary to disease of the spinal cord.

Hence, as a working hypothesis, we have come to the loose and tentative formulation hinted at by Dr. Milhorat, namely, that a defect in the metabolism of creatine is an index of the mass of improperly functioning muscle. This may be restated as follows: If one looks on primary myopathy as evidence of a general disturbance in the metabolism of muscle which affects all or most of the muscle tissue of the body, a slight or barely visible atrophy could be accompanied by a severe disturbance in the metabolism of creatine. In contrast, in wasting secondary to disease of the spinal cord, the metabolism of creatine could be less or only slightly disturbed, because, although certain muscle fibers are completely destroyed by the disease, others are perfectly adequate and completely functioning. In other words, even in muscle bundles severely wasted as a result of disease of the spinal cord there may be a certain number of perfectly sound muscles besides those uninvolved muscles elsewhere in the body. In muscles less severely wasted in a disease of general metabolism of muscle all the fibers may be seriously affected chemically although not visibly altered.

Surprising to us is the fact that myotonia congenita, presumably a primary myopathy, has a metabolism of creatine, as far as these criteria go, that is normal. Also surprising is the fact that myotonia atrophica, a disease which clinically in some ways resembles dystrophy more closely than anterior poliomyelitis, more closely resembles the latter type of syndrome as regards the metabolism of creatine.

Glycine, as mentioned, may be tentatively looked on as an amplifier or magnifier of the defect in the metabolism of creatine, or more specifically in tolerance for creatine. It is as though a defective muscle just about able to carry the load put on it by the creatine tolerance test shows its inadequacy when it has to manage both creatine and glycine. Hence the problem of metabolism of creatine is still

a knotty one. The chemical investigation must go much further to give an adequate understanding of disease of the muscles.

DR. A. T. MILHORAT: No adequately controlled observations on the elimination of creatinine following amputations have been reported. The statement is frequently made that following the amputation of a limb or even of two limbs the output of creatinine is not diminished. However, when one studies the protocols from which this conclusion has been drawn one finds, first, that no observations were made before the amputation and, second, that the amounts of creatinine excreted actually were lower than those observed in normal persons of the same age, sex and muscular build. In determining whether the elimination of creatinine by such patients is normal or abnormal, the total output of creatinine must be used as a basis for comparison. Obviously the use of the creatinine coefficient, which is the ratio between the output of creatinine and the body weight, can lead to erroneous conclusions.

It is true that the excretion of creatine can be influenced by large variations in the intake of nitrogen.

The effect of glycine on creatinuria is not due to the nitrogen contained in the glycine. Dr. Brand showed this some years ago. Nor is the effect of the glycine on the tolerance for creatine due to the nitrogen content of the glycine. Both effects are out of proportion to the amount of nitrogen in this amino-acid. When equivalent amounts of other nitrogenous substances (such as protein) are substituted for the glycine, the effect on the excretion of creatine and on the tolerance for creatine is slight.

The use of glycine in the therapy of progressive muscular dystrophy will not be discussed at this time, except to point out that in patients with this condition the effect of glycine on the course of the disease is influenced by many factors. Prominent among these factors are the amount and functional capacity of the muscles still remaining. In evaluating the therapeutic effects of glycine in patients with progressive muscular dystrophy one must distinguish between the patients who show the least amount of muscle disability and in whom progress of the disease has been slow and those in whom the muscle wasting is extensive or the course of the disease is rapidly progressive. Unfortunately, some investigators have not given adequate attention to these factors. There appears to be sufficient evidence that glycine is of considerable value in the treatment of many patients with myasthenia gravis. It is postulated that glycine probably acts as a precursor of creatine or creatine-phosphoric acid in the muscles. Ephedrine, on the other hand, probably increases the rate or resynthesis of the phosphocreatine.

From the studies of the metabolism of creatine in cases of myasthenia gravis it is believed that the actions of ephedrine and glycine are different but that their effects are similar. When glycine and ephedrine are given together, a summation of effects is usually observed.

EXPERIMENTAL ANALYSIS OF THE FUNCTIONS OF THE FRONTAL ASSOCIATION AREAS IN PRIMATES. DR. C. F. JACOBSEN, New Haven, Conn. (by invitation).

Clinical observations of cases of extensive injury to the frontal association areas indicate that there is severe deterioration. Brickner has suggested a unitary explanation for these diverse emotional and intellectual disturbances, namely, an impairment in the elaborate synthesis of the simpler engrams produced in the more posterior parts of the brain.

The extirpation of the frontal association areas in monkeys and chimpanzees causes behavioral disturbances strikingly similar to those described in man after similar lesions. In the present experiments the functional equivalence of symptoms referable to the frontal lobe in man and in the chimpanzee has been used to pursue an experimental analysis not possible in man.

The aims of the experiments have been twofold: (1) to determine the conditions under which synthesis fails and (2) to indicate some of the characteristics of neural organization underlying these responses. Two adolescent chimpanzees were trained on a series of problems which made varied demands on their

capacities. Each animal's ability to use sticks in order to obtain bits of food beyond its unaided reach was tested under two conditions: (*a*) The essential features of the experiment were arranged within the animal's visual field. Thus the animal might be required to use a single stick to reach a piece of food which had been placed slightly beyond its reach; or in more complex situations, the animal might be required to draw in the nearer of two sticks and use it to get a longer stick, which could then be employed to obtain the food. (*b*) In the second series of tests a stick was placed on a platform at one end of the work cage and a bit of food on a platform at the opposite end. The two platforms introduced a factor not present in the single platform tests, namely, a temporal organization of behavior. The necessary elements were not available in the immediate visual field, but the sight of the food on one platform had to be supplemented by memory of the stick on the other platform.

Bilateral extirpation of the frontal association areas did not significantly alter the animal's manipulation of the problem when the essential elements were presented in the animal's immediate visual field. However, adjustments to the two platform situation involving temporal organization of behavior were severely disturbed, and at no time was there evidence that the subject appreciated the presence of food on one platform and of a stick which could be used to obtain this food on the other platform.

Temporal patterning of behavior was further studied in a test situation which gave opportunity at various steps of the problem for the subject to make either one of two mutually antagonistic responses. However, in order to effect a solution of the problem the animal had to learn to hold one of these reactions in abeyance until a particular point in the sequence of acts was reached. This patterning of responses was mastered by the normal animal; unilateral extirpation of the frontal area made no material change. Bilateral extirpation, however, seriously disrupted this patterning of behavior, and in the case of the animal with the more extensive lesion, postoperative reeducation did not reestablish the habit.

In tests of recent memory the animal was given an opportunity to observe the experimenter conceal a piece of food under one of two cups, and after an interval of delay ranging from a few seconds to several minutes the subject was allowed to choose between the two test objects. Since the external appearances of the cups gave no clues to a correct choice, it was necessary for the animal to remember under which cup the food had been concealed.

Unilateral lesions had no effect on performance in these tests. When both frontal areas were removed the subjects were completely unable to respond when the food was hidden for only one or two seconds. This stands in contrast to the excellent performances after delays of several minutes when the animal was normal and after the removal of one frontal area. There was no indication of hemispheral dominance.

The test of recent memory was also used for studying the animal's emotional adaptations. Before operation it was not uncommon for the subject to cry and at times have violent temper tantrums when it made incorrect responses. By training on problems in which errors were frequent and which were too difficult for the animal to master it was possible to produce an "experimental neurosis." Bilateral extirpation of the frontal areas resulted in marked changes in affective responses. The chimpanzee no longer was disturbed when it made a mistake; when confronted with problems beyond its range of ability, it repeatedly tried the task, but at no time was it possible to evoke even a suggestion of an "experimental neurosis."

The test of recent memory was used with monkeys in making a further analysis of the neural correlates associated with this function. As in the case of the chimpanzee, bilateral extirpation of the frontal areas resulted in a complete loss of this ability. Partial lesions reduced the length of the memory span rather than abolishing completely this particular function. This failure cannot be regarded as a generalized deterioration of intelligence, since learning and performance on problems not requiring "recent memory" were normal.

Other areas of the cortex were explored to determine whether the memory defect was peculiar to the frontal association areas or whether it could be detected after extensive lesions in other regions. Bilateral injuries, in different animals, of the parietal association areas, of the motor and premotor areas, of the temporal lobes and of the postcentral convolutions (Breslow) resulted in no impairment of recent memory. Extensive postoperative reeducation failed to reestablish this function.

It is concluded that after bilateral injury to the frontal association areas those activities which in their very nature demand integration over a period of time can no longer be effectively carried out. The subject seemed unable to remember a single experience for even a few seconds in the face of new incoming sensory data, and temporal patterning of responses necessarily failed. This defect cannot be attributed merely to an extensive injury of the cortex; on the contrary, the specificity of the frontal areas in respect of this function is proved.

DISCUSSION

DR. FREDERICK TILNEY: I wish to congratulate Dr. Jacobsen for this excellent presentation of a clearcut series of experiments and to thank him for his appreciative reference to Richard Brickner's recent work, which in my opinion is one of the most penetrating and painstaking studies of the function of the frontal lobe that have been made. Dr. Jacobsen has carefully safeguarded his position in drawing analogies between animals of different species, and particularly in this case between primates and man, except in one particular, that is, when he spoke of the neuroses of behavior in one of his chimpanzees when presented with certain frustrations in his experimental set-up. It may be that he is correct in this, but I think the matter needs careful definition as to exactly what is meant by neurosis. I am certain that in children one constantly observes refractory phases in which the child refuses to do something that it has previously been trained to do perfectly well during a certain period of development. It may be, as I said, that one is justified in calling this a neurosis, but for my part I should use much reservation and care in making any such analogy.

When one comes to consider the function of the brain and certain new conceptions presented, one needs to focus thought pretty finely in the matter of the frontal lobe, which has always been such a *bête noire;* it has been debated one way or another for the last century, and in one of the latest decisions it was regarded as a silent area. Now it is beginning to be learned that it is not a silent area at all, but a very eloquent area and sometimes a very noisy one. From the experiments presented it is clear that certain new things have come to light as a result of Dr. Jacobsen's work; the sequence and patterns of behavior and what he calls the temporal organization of behavior; then the smooth flow, particularly of recent memory, and the ultimate adjustment of the individual organism to the environment. These, it seems to me, are all new conceptions, and while one must be careful in transferring their application from even the high primate, such as the chimpanzee, to man, nevertheless they have a great deal of significance for clinical interpretation. I think, however, that in spite of these excellent experiments neurologists are still groping in this matter of cortical interpretation. They are groping because they have accustomed themselves to think in topographic terms and not in cytologic terms; I say this with a great deal of feeling as one of those who are constantly surveying the cortex in all of its divisions and trying to understand what is going on in that part of the nervous system. I must confess that while experiments of this sort lead me to certain inferences with reference to localized function, they satisfy me not at all in understanding how these functions are brought about, and I have been bold enough to make the statement that if one does not know yet all the functions of any single cell in the cerebral cortex, how therefore can one interpret the activities of such a great organ? I think that neurologists are groping also when they condescend to use such a symbolistic term as equipotential, or equipotency, as applied to different areas of the brain. It seems to me astonishing that one can, in view of the great

histologic differences, seen easily enough, yield to the temptation of speaking of areas, even though near together, as equipotent. With time, I think, and more microscopic knowledge and also a knowledge which would be, if I may use the term, more microphysical, one will see how much advance has been made by means of experiments like these, but there is a great distance to go yet. It is not less of these experiments that is needed but more of them; their own limitations will show how much more is needed to understand the minute structural organization of the cortex. This communication of Dr. Jacobsen has inspired me to go back to my work, particularly as it applies to the frontal lobe, with renewed impetus, in the hope that I may obtain some further light on that part of the brain.

DR. RICHARD BRICKNER: The observations of Dr. Jacobsen are notable for their accuracy, systematization and restraint in interpretation. If I recall the literature correctly, no experiments have been made which compare with his in these respects. The most elaborate ones, which perhaps run second, are those of Bianci, although his interpretations are chiefly those of effect, and I do not believe that they rank with Dr. Jacobsen's in scientific point of view. This work indicates that progress has been made beyond the stage of a decade ago, when the frontal lobes were regarded as a group of centers for many different forms of specified activity. As recently as 1922 there were considered to be a murder center and an arson center and regions functioning for many lesser forms of crime.

I wish to ask Dr. Jacobsen what he thinks of the striking differences between the effects of unilateral extirpation and those of bilateral extirpation. This is one of the phases in which the results after operations on the chimpanzee resemble those following extirpation in man. After unilateral extirpation in human beings there are few or no pathologic results. It is the first time that so clear a resemblance between animals and man has been possible. The question is whether this fact does not imply a twin representation of function, of engrammic processes in the frontal lobes.

DR. E. D. FRIEDMAN: Dr. Jacobsen remarked that his animals were just as eager after operation to carry out whatever acts they had been taught to do as they were before operation. I wonder, however, whether he noted in any animal the symptom which has been described as frontal akinesis, a disinclination to carry out voluntary acts. I wish also to ask whether he would interpret the confusion, or neurosis, which he produced in some animals as being in the nature of a loss of the *Gestalt* with failure on the part of the animals to sense adequately the constellation in which they carried out these acts, a concept which Koehler, Koffka and Goldstein have thought so important in the process of learning and the mechanism of memory.

DR. CARLYLE F. JACOBSEN: With regard to Dr. Tilney's wise caution on the use of the term neurosis, may I say that I used the term experimental neurosis in a descriptive sense as it was applied by Pavlov rather than in its human clinical connotation?

With regard to Dr. Brickner's question on the relation between the unilateral and the bilateral effects, certainly at the present time I think the notion of a twin representation in the two hemispheres, at least so far as function of the frontal area is concerned, is acceptable. This is a problem in which I have been particularly interested, and we are now attempting a further series of experiments dealing with sections of the corpus callosum and controlling the sensory inflow to a given hemisphere so as to be able to elucidate that factor further.

With regard to the question of slowness in initiating activity, we have not encountered that disturbance when a lesion has been confined strictly to the frontal zone area. If the lesion includes a considerable portion of the premotor area, then we have noted a distinct retardation in the readiness with which an animal can initiate activity and likewise a tendency toward perseveration, even though the cause for the activity has been removed for some time.

I have not attempted to formulate the problems in terms of *Gestalt*, but I think that it is evident that the same materials which I have been dealing with here

could readily be translated into *Gestalt* formulations of the problem. Under those conditions it would be a failure of the temporal *Gestalt* rather than of the spatial *Gestalt*, such as one sees in the perception field.

SOME SIDELIGHTS ON THE PSYCHOLOGY OF MURDER. DR. GREGORY ZILBOORG.

For almost a century sociologists have been pointing out that there exists a definite relationship between suicide and capital crime. The sociologic studies of Lacasagne, and later those of the Italian sociologic school, particularly of Ferri and Morselli, seem to prove that the statistics for suicide and homicide run in an inverse ratio. This is true not only with regard to general statistics but also with regard to the geographic distribution of suicides and homicides. Thus Catholic countries, such as Italy, Spain and Ireland, show a definite preponderance of homicides with comparatively few suicides, whereas in Protestant countries the rate of suicide is comparatively higher and the rate of homicide is correspondingly lower. The same relationship can be observed in various parts of the same country; thus, southern Italy shows a preponderance of homicide over suicide, while northern Italy shows an opposite ratio. Despine calculated that in fourteen departments of France in which capital crimes were frequent there were only thirteen suicides per million of population, while fourteen other departments with fewer murders showed the rate of 83 suicides per million of population. In the department of the Seine murder represents 17 per cent of all indictments, with 427 suicides per million of population, whereas in Corsica the incidence of capital crimes is 83, while that of suicides is 18, per million. Suicide and homicide are apparently psychologically related entities. However, it would be difficult, if not impossible, to try to fit every suicide and every homicide into any one of the known psychiatric pigeon-holes. Clinical studies of neuroses and psychoses and careful psychoanalytic studies of both of these psychopathologic groups seem to indicate that suicide is not always a result of what is known as pathologic depression. A study of prison material leaves little doubt that there are a number of homicidal persons who are not criminals from the sociologic point of view, although they are no doubt criminals from the standpoint of the law. By this is meant that a certain number of homicidal persons who finally serve sentences in prisons are apparently first offenders whose crime has been motivated primarily, if not wholly, by a prolonged and almost uninterrupted chain of unconscious motivations which are never disclosed at the trial because of the limitations of the present legal procedure. A clinical study of some murderers in Sing Sing Prison in Ossining, New York, seems to warrant this conclusion. Illustrative cases may be cited: An Italian plasterer, in his late thirties, was the father of a large family, and the small son, who was his favorite, was taken ill. The physician gave an injection, following which the child died within a few hours. The physician did not return until the child was dead and its body laid out. When he came in the father met him shouting, "You have killed my boy." The physician was taken aback and asked the bereaved father to step into the next room with him, where he implored him not to make so much noise and offered to pay the funeral expenses of the dead child. This incensed the father who, shouting, "I am an Italian man," "knocked the doctor out." He then ran into the kitchen, seized a knife, returned and stabbed the unconscious doctor in the throat. It was only when he saw blood that he calmed down somewhat and declared to his family that he had killed a man. He left the house, went to his older brother, who lived miles away, told him what had happened and decided to hand himself over to the police. The man was convicted and sentenced to death; he spent ten months in the death house and was then granted a new trial, following which he was given a long prison sentence. He proceeded to lead the same life of an honest plasterer within the prison walls as he had done outside them. A study of this criminal easily disclosed the complicated network of emotional motivations which led him to murder in what appeared to be undoubtedly a state of uncontrollable affect. The purely external consideration of the facts nevertheless led the law to say definitely that while premeditation existed legally it did not exist psychologically.

Another much more complicated case is that of a young man who committed murder in what appears definitely to be a state of fugue. He killed a taxicab driver, took possession of the cab, later disposed of it and disappeared. He was not apprehended until six years later, during which time he had led the life of an honest worker and had married and lived happily and peacefully with his wife under an assumed name. While vaguely aware that a crime had been committed, he was completely amnesic as far as the act itself was concerned. A prolonged study of the case, lasting many months, revealed an unusually complicated life. Since childhood the boy had been interested in mechanical things. He had wanted to drive the family automobile, which was forbidden to him. The family had always imposed decisions on him as to studies, career and everything else. When one day it was announced that the family decided that he was to study medicine, he became low in spirits and was found that evening tinkering with the carbureter of the family car. Now, while serving a life sentence in prison, he is one of the best, most industrious and most capable automobile mechanics of the institution. His life was a mixture of a great desire to settle down and of peculiar truancy. Many details of his childhood were reported. His dreams, as well as other data presenting unconscious material, were cited. The whole crime was reconstructed as a sudden impulsive acting out of the murder of his father, as well as of a psychotically imagined suicide through the murder of the taxicab driver. Incidentally, a great part of the man's amnesia of the crime was cleared gradually in a piecemeal fashion during the course of many interviews.

It seems that in the present state of knowledge one is justified in postulating the existence of neurotic homicidal criminals who from the standpoint of traditional psychiatry would be considered asymptomatic. Their crimes are a final catastrophic outgrowth of their respective neuroses, and there is more than a justified suspicion that such criminals could be treated and a great many of them apparently cured. This treatment would be the most effective method of prevention. Under the present criminal law such treatment is possible only within the walls of the prison. Effective and prolonged treatment might later require some change in the parole system. It is of great importance, however, to bear in mind that psychiatric knowledge of the psychology of the criminal is as yet extremely limited and to the general public and the judiciary highly unconvincing. Moreover, to arrive at a real understanding of the criminal, he must be studied for a long period of time. Hence the prison presents the best clinic where therapeutic efforts can be applied. Any radical reform in the whole system should start with psychiatric studies of criminals rather than with the reorganization of the prison systems on the basis of pure psychiatric theory.

DISCUSSION

DR. VERNON C. BRANHAM (by invitation): The excellent work which Dr. Zilboorg has been doing at Sing Sing and at Bedford Hills, I believe, represents the third organized attempt to establish psychoanalytic procedures in connection with the field of crime. I am thinking of Alexander's work in the Massachusetts State Prison and of Karpman's work with the criminally insane at St. Elizabeth's Hospital. This is a field in the correction of crime that has been sadly neglected. Analysis of the criminal make-up should become a regular organized procedure in the prisons. Unfortunately several things mitigate against the pursuit of such studies. The wardens, for the most part, are not in sympathy with this type of work. They cannot understand why a man should spend hour after hour, week after week, on a single case, when there are perhaps a dozen or a hundred such cases in the institution. Furthermore, the psychiatrist receives a salary considerably higher than the principal keeper, and the warden cannot understand why that should be so. I suggest that an institute for the study of crime be established, not with the idea of crime prevention, such as the Crime Prevention Bureau of the New York City Police, nor for the apprehension and detection of criminals, such as that suggested at the recent Crime Conference in Washington. Such an

institute should have many of the functions and a set-up similar to that of the New York State Psychiatric Institute and Hospital in the department of mental hygiene. The suggestion is made that such an organization be empowered to select material from new prisons, to retain these persons as long as is necessary for proper analysis and study and then to turn them back into the prison system itself. Until something of the kind is done criminal conduct will not be understood. About as much as can be carried out with the present set-up is the study of the social aspects of crime, and that is delimiting the subject rather severely.

Coming more specifically to the last case which Dr. Zilboorg mentioned, I had an opportunity to talk to the young man at Sing Sing two or three times, and I have studied his case history. My notes coincide to a remarkable degree with the conclusions drawn by Dr. Zilboorg. There are one or two additional characteristics about this case, however, that should be mentioned. The mother was domineering and really the "boss" of the family. As a fact, the patient himself so characterized his mother. She was the one who prevented him from doing the things that he wanted to do. That developed in him a sense of frustration which he never entirely overcame. He was forced to go to Syracuse University Medical School and at the same time was forced to live at home under the dominance of his mother. As Dr. Zilboorg pointed out, he tried to escape from this situation by running away from home on several occasions. Later he actually ran away from home and proceeded to get into trouble immediately. When he was 19 years of age, in the navy, he was involved in a saloon brawl in South America and was struck over the head with a bottle. Following this, he and his parents state emphatically that he suffered from dizziness, prolonged headaches and periods of depression. To my mind this is analogous to the frequent statements that a patient had a fall on his head when he was a baby. One is inclined to read a great deal into such traumatic accidents. There is nothing in this symptom complex that indicates true epilepsy or even an epileptiform reaction. The boy was discharged from the navy dishonorably for stealing an automobile, and then he began a wandering sort of existence, going back and forth over the country. This boy is the oldest of five children; the father is a graduate of Princeton, successful, wealthy and influential; two siblings are happily married; one is holding a good position, and one is a successful student in Princeton. The boy himself was precocious. He gave every promise of fulfilling his father's best wishes; instead he did not accomplish any of the things that his family thought he should. At 16 he ran away from home. Later he enlisted in the navy with the idea of becoming an air pilot, but he was unable to do so. Dr. Zilboorg has called attention to a significant conversation between the father and the boy shortly before the murder. I did not know the exact content of this conversation, but Dr. Zilboorg's remarks throw considerable light on it. There was only one way in which this boy could resolve the conflict in the light of what he had heard from his father, namely, the annihilation of the father himself. It is interesting that at the time the interview took place the boy refused to see his mother. He was willing to talk to the father; I think that the father's scoldings destroyed the illustration that the boy had in the omnipotence of the father and perhaps gave him some idea for the first time of actually carrying through the fantasy that began at the age of 12, which Dr. Zilboorg has mentioned. The loss of memory of the crime itself has been mentioned. There was a loss of reality there, and the state of fugue lasted for a period of several hours, until the boy had actually disposed of the automobile itself. I consider the killing of the taxicab driver to be, psychologically speaking, suicide, and to accomplish two purposes. First, in the boy's subconscious mind, by ridding the father of the boy the mother would be appeased, and all of the dissension which seems to have grown out of the mother-son situation would be settled by the "death" of the boy; second, it would wipe out his previous existence, his so-called bad period of life, and he could begin anew. Following the murder a complete catharsis seems to have taken place. There was a marriage which seems to have been fairly satisfactory. For the first time the young man secured good positions and was promoted. He showed a great deal of intelligence and was well thought of, and

to every intent and purpose he was living a new life. Psychologically, the "suicide" had accomplished the purpose of doing away with the old life and bringing a new man into existence.

There are several ways in which the conflict could have been solved by this man. The first is by engendering a feeling of hate, a sense of betrayal on the part of his mother, which could only be solved through revenge. In such a situation the boy would have murdered his mother and not the surrogate of his father. A second type of resolution would have been secured if there was a strong sense of humiliation, a totally passive attitude toward the situation; this would have resulted in a badly inadequate personality, and he would have probably taken to drugs or alcohol. A third possibility of resolving the conflict is the development of an anxiety neurosis, having as its source deep feelings of conflict and the need for retribution. Finally there is the possibility of a symbolic regaining of the love-object through the death wish, and that is, to my mind, the way this particular conflict was solved. I wish to reiterate that this case opens the possibility of doing a great deal of similar work with many other cases of murder in the correctional system.

DR. ISRAEL STRAUSS: I first want to comment on one statement made by Dr. Branham. There are psychiatrists in most of the correctional institutions of the state, and apparently what Dr. Branham wants is to have psychiatrists with psychoanalytic training. But he says that the money is not available, and the wardens are jealous of the psychiatrists. Is this not ridiculous in view of the fact that the wardens of the state institutions receive $9,000 a year and maintenance and the medical directors in the hospitals for mental disease receive $6,000 a year and maintenance? I do not see why the wardens should be jealous.

I was much interested in the data given by Dr. Zilboorg regarding suicide and homicide. Dr. Zilboorg is an erudite student. I wondered why all his figures for homicide and suicide came from the years 1878 to 1885. It would have been interesting to have figures of more recent years, since such different conditions have arisen during the last twenty years. I wonder if the same ratios have persisted in this country and others up to the present time. I do not know whether the figures are available, but it would be extremely interesting to have them.

The first case which Dr. Zilboorg told us of, that of the Italian father, is interesting. He showed how the Italian could not take money for his dead boy. The thing that struck me was that by offering to pay for the burial of the boy the physician expressed a sense of guilt which seemed to the poor Italian a confession that he had committed murder. To me, that admission of the physician was a more powerful motive impelling the father to kill than the thought that came to his mind "I cannot take money for my dead son." The physician really sealed his doom with that statement. It is interesting to know that this man has been in the penitentiary ten years for a crime of passion of that type. At a meeting at the Bellevue Hospital a few years ago, an Italian was presented by Dr. Gregory with the following story: The man was married. The father-in-law did not approve of the marriage and continually "picked on" his daughter. He hated his son-in-law so much that he made life miserable for the couple. One night the father came to the house where these two people had been living happily and forced his way in. The husband shot the father dead. He was in the hospital, evidently for the purpose of determining his sanity. No one could find any indication of mental disease at that time. The man himself stated that he realized that he had had no right to kill and would probably have to be punished for his act. I believe that the opinion of many of the men sitting in that audience was that the man had to be punished and go to prison.

Dr. Zilboorg closed the account of his second case with the statement that the man was and still is neurotic and cannot be considered cured until he is treated. I wonder whether Dr. Zilboorg's handling of him is not treatment in one way. Psychoanalytically, a form of treatment is free association. Also, I wonder whether Dr. Zilboorg claims that this man has committed psychic suicide; in killing his father-image he has really killed himself and freed himself; so why

is he not cured and adjusted? Do not his life in the factory and his successful married life demonstrate that he has freed himself by having "killed" himself, thus leading to a successful adjustment? If I understood Dr. Zilboorg correctly that he had really committed suicide, can a person who has committed suicide commit it again?

My next point refers to the case of the Italian who killed the physician. Had the Italian merely struck the physician down and killed him he would have been guilty of homicide—manslaughter, a death committed in passion without premeditation—but because he left the man after striking him down, went to the next room, seized a knife and came back and stabbed him, it became murder in the first degree, in other words, murder with premeditation, because the Court of Appeals in this state has held that it takes but a minute for the development of premeditation. Psychologically, all will agree that the underlying impulse in this man which caused him to knock the physician down was the same impulse which led him into the kitchen to get the knife; yet the law fails to recognize this fact. If he had been successful in killing the man with a blow on his head he would have been sentenced for from twenty years to life, but because he went into the kitchen and afterward stabbed him the penalty became death. That is what psychiatrists are facing in the interpretation of the law in this state. Furthermore, how much weight would be placed on Dr. Zilboorg's analysis if he were called before the court in the defense of the young man who killed the taxicab driver and explained the motivation impelling this man to murder? What attention would be paid to him? I will cite another example: A man named Fish was indicted for the murder of a child. All abhor such a terrible crime. A number of years ago a federal judge, Judge Coleman, had to send Fish to the psychopathic division of the Bellevue Hospital for a test of his sanity, and it was stated in the newspapers that Dr. Gregory reported that the man was psychopathic but that he was sane, because he knew the nature and quality of his acts. Every one knows that this man is psychopathic, that he is probably a sexual pervert and that he is impelled by uncontrollable compulsions. I do not doubt that he has an obsessional neurosis. When one reads in the papers that needles were found in his stomach and body it would not take much for one to commit him to a state hospital. Two able psychiatrists were called in, Drs. Lambert and Vavasour, who declared the man to be sane. Why? Because they were put face to face with that statutory definition that cannot be escaped. There are about eighteen states in the United States that recognize that an irresistible impulse, if it can be shown that it is an enduring and not a momentary one, is a definite defense for murder, and that the afflicted person is not responsible. There is nothing like this defense in New York. In fact, the law holds that uncontrollable impulse is no defense. A person with kleptomania or pyromania cannot be defended on the basis of insanity in this state.

Dr. Zilboorg says that these patients should have treatment. They should have treatment, but one ought to have the right in the first place to select persons who require treatment and not electrocution or punishment beyond the desserts of their crime. Whether one or a dozen murderers in Sing Sing or any other prison are analyzed, it will not have any effect on the public until neuropsychiatrists of this state get together and point out to the public the injustices of the statutory limitations under which neuropsychiatrists labor when they try to advise justices. Such an analysis as Dr. Zilboorg has made is of great scientific importance. He would not be the one to say that he is getting at the causation of crime by the analysis of an individual criminal. He knows as well as I do that the causative factors of crime are many. What he is doing is studying the psychology of such a man and showing definitely those abnormal mental processes which control him or interfere with his acting as a social being. This work is of tremendous importance.

DR. GREGORY ZILBOORG: As far as Dr. Branham's appeal goes, I shall make the first generous contribution toward the project by presenting him with all the good will in my possession. As to the various details in the case given by

Dr. Branham, I was reluctant to cite too much of the data. As I said on another occasion, the civil restoration of the young man is not excluded as a possibility, and I preferred to make public as few of the flagrant details as possible. The man under discussion had a severe neurosis. One of the deepest sources of his trouble was the relation to his sister. Up to the age of 16 he was addicted to a peculiar, purely domestic kleptomania. Apparently there was some slip in the transcription of the information obtained by Dr. Branham. The crime for which the future murderer was discharged from the navy was a queer one. At the age of 17, acting on pure impulse, he took the jacket of another sailor which had golden buttons. An officer noticed it. The boy was arrested and spent a year in naval prison. Between the ages of 3 and 15 he would steal pennies—only pennies and only from his mother's pocketbook.

As for the statistical data collected: up to 1880 French and Italian students of the problem of the psychology of murder did a good job, and I had little to do to compile and finish the tabulation of the facts, but the statistical data from 1880 to 1910 have not been tabulated. That I must do myself and can only report progress. In the last twenty years, with wars, revolutions and other disturbances, such confusing relationships have been produced that a clearcut conclusion could not be derived from a study of this period. I believe that the study of homicide and suicide and the correlation of these two phenomena should be pursued.

Dr. Strauss remarks about the need for a serious change in the criminal law lead me to conclude with a historical reference. I do this not to deprive Dr. Strauss and his collaborators of the credit of originality but only to reenforce them with the weight of historical precedent. In the city of Metz, in the year 1520, there lived a physician who at one time had studied magic and owned a black French poodle dog. He was suspected by many and so was his dog—the latter of being the devil and the master of being the wizard. This man, at the risk of his life, appeared in court demanding the release of a poor woman who was being tortured and about to be sentenced to the fire for being a witch. Many years had passed before the criminal law of that day was changed, but when the protesting physician passed away there were people who said that they saw the dog yelp, jump off the bridge and drown because the poor devil had nothing else to do when Cornelius Agrippa died.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

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C. A. McDonald, M.D., *in the Chair*

Primary Degeneration of the Corpus Callosum: Report of a Case with Autopsy. Dr. Lester S. King.

This case is one of degeneration of the corpus callosum of the type first described by Marchiafava and Bignami in 1903, and it is the first to have been observed outside of Italy. The patient, an Italian aged 54, showed symptoms of mild mental deterioration for about three years, with clumsiness, slight ataxia and slight spasticity for from four to six months. He sank into stupor about two days before entering the hospital. There was no history of addiction to alcohol.

Autopsy showed symmetrical areas of degeneration in the corpus callosum and the centrum ovale. The principal features of the microscopic picture were: loss of myelin with preservation of axis-cylinders, numerous gitter cells, marked progressive changes in the microglia and oligodendroglia, absence of gliosis, marked clasmatodendrosis, absence of all inflammatory signs, great apparent increase in vascularity and moderate proliferation of reticulin.

DISCUSSION

DR. J. B. AYER: I have not seen a case of this kind before. Although the circulation is not obviously at fault here, when one sees symmetrical lesions one thinks that it may be. Can there be any ischemic process here? I should like to hear more about apraxia in a case of this sort.

DR. H. R. VIETS: I am disappointed that one cannot learn more about the function of the corpus callosum from this case. There is some clinical evidence that part of the fibers from the motor area pass through the corpus callosum and the results of physiologic experimentation seem to bear this out. Fibers from the premotor area, however, probably do not pass through the corpus callosum.

DR. T. J. PUTNAM: This case is a course in neuropathology in miniature. Several important pathologic processes involving the white matter are represented. I feel a special interest in that the most striking feature is a fairly specific loss of myelin, with only inconspicuous areas of loss of axis-cylinders, both of a degree comparable with those seen in cases of multiple sclerosis. The feeling is growing at the laboratory of the Neurological Unit that demyelinization of this type is a fairly specific response to vascular obstruction. Evidence of such obstruction may be found in cases of multiple sclerosis, "postinfectious encephalitis," some types of diffuse sclerosis and dementia paralytica, and a similar histologic picture is seen following venous thrombosis and experimental venous obstruction. In Dr. King's case there are evidences of vascular abnormality, and the inflammation is comparatively slight. The lesions have a similarity to those of Binswanger's subcortical *encéphalite*, an obvious vascular disease with demyelinization but without the distinctive localization seen in the present case. The almost complete absence of glial fibrosis suggests perhaps a nutritive disturbance, as in cases of pernicious anemia.

DR. D. GREGG: Was there any symptom that was unilateral, either a motor or a sensory change? From study of the brains of various animals, my understanding is that the area of the corpus callosum develops with the development of the anterior lobe. Perhaps that explains why symptoms are psychopathic rather than motor.

DR. H. H. MERRITT: I wish to ask Dr. King if he was able to determine from his study the approximate age of the lesion in the corpus callosum in this case? In the lantern slides there was a large number of compound granular cells. When these cells are present in such large numbers it has been my impression that the lesion is acute and that it probably is of vascular origin. Is it possible that the lesions in this case represent the result of vascular lesions which occurred at the time the patient sank into coma five or six days before death? Critchley, in a study of the anterior cerebral artery, suggested that Marchiafava's syndrome may be due to a lesion of the branches of the anterior cerebral artery which supply the corpus callosum.

DR. L. KING: I wish to apologize for the inadequate history, but I did not see the patient, who was in the surgical service, where the neurologic symptoms are not the interesting ones. The patient was absolutely uncooperative while in the hospital, and no tests could be carried out. The clinical history given by his son was not especially reliable. I think that will answer Dr. Ayer's question concerning apraxia. It was impossible to determine whether it was present. The question of blood supply was raised by Dr. Putnam. The main arteries were normal. As to involvement of the finer blood vessels being responsible for the disease, I could not find any thrombi or obliteration of the lumen by fixed elements. However, it is significant that there was a certain amount of proliferation of connective tissue through the brain in the form of fine strands of reticulin. What repair there was took place by a very slight fibrosis and not by gliosis. The absence of glial response was the puzzling feature of the disease. The point of the age of the lesion was brought up by Dr. Merritt. They extended over a long period of time. I say this with the literature in mind. A great number of gitter cells is not necessarily a sign of a recent lesion. A case was reported in the

literature in which in a bullet wound of twenty years' standing large numbers of gitter cells still remained. There was no proliferation of glia fibers, but there were small cysts and cavities. Loss of tissue was replaced by fluid. Dr. Putnam mentioned the possibility that a nutritional factor was responsible for the absence of gliosis. Patients frequently show marked nutritional disturbances in this disease and often die of marasmus. I do not know whether the relation is one of cause or effect, but there is a close connection between marasmus and this disease. My patient lost 15 pounds (6.8 Kg.) in a short time. This is a significant amount. As to Dr. Viet's question about the premotor area, there is loss of instinctive control. These features may well be due to involvement of the frontal lobe in the degeneration. The sections showed a slight widening of the perivascular spaces. Other abnormalities bore no relation to the principal disease process. I thought that the cyto-architecture was normal. There was no particular gliosis in the cortex. The frontal area of the cortex, as well as other areas, showed nothing of significance. Dr. Gregg's question about the psychiatric symptoms is borne out by the fact that in the literature the anterior portion of the corpus callosum was always involved while the posterior portion was not always involved. In reply to Dr. Ayer's suggestion that the symmetry of the lesions is an argument for a vascular basis, it would be difficult to accept that, as the lesions reported are so widely separated. There have been reported lesions throughout the white matter of the entire cerebrum. They were widely symmetrical. I do not know of any single blood vessel the involvement of which could cause so wide a separation of lesions. If one is to accept a vascular basis at all, it would be necessary to place the onus on numerous small vessels in which thrombi might be very difficult to find.

REFLEX ACTIVITY WITHIN THE SYMPATHETIC NERVOUS SYSTEM. DR. HENRY G. SCHWARTZ.

Leriche in 1928 collaborated with Fontaine in a report on vascular responses. Since sections of the spinal nerves plus sympathectomy seemed unavailing in bringing about relief from pain, they claimed that some unfamiliar mechanism must be at work. Several years previously Foerster observed that pain persisted and deep sensation returned following section of the dorsal roots of the peripheral nerves. Leriche and Fontaine postulated five types of reflexes controlling the activity of the blood vessels, viz.: (1) "intramural," (2) axon, (3) intraganglionic autonomic, (4) medullary and (5) cerebral. Leriche found that after sympathectomy and spinal neurectomy the blood vessels of the denervated extremity still reacted to external application of heat and cold. By ruling out an axon reflex, he maintained that the reaction was produced by afferent and efferent fibers passing through a center within the wall of the vessel—an "intramural" reflex. So far as the axon and medullary reflexes are concerned, there is ample evidence for their existence. That leaves, then, only the reflexes of the third and fifth types, i. e., intraganglionic and cerebral, devoid of conclusive evidence. The arguments concerning the presence of the third type, together with the bulk of the report which I am presenting, have appeared in the *American Journal of Physiology* (**109**:593, 1934).

DISCUSSION

DR. GEORGE WISLOCKI: I have little to remark concerning this exceptionally interesting physiologic exposition. The findings offer rather conclusive proof that reflex impulses are mediated through the stellate ganglion, in other words, that there are true sympathetic reflexes requiring no central connection. It would be interesting to supplement the physiologic demonstration by an anatomic study of the pathways involved.

DR. S. COBB: I wish to ask about nicotine. Does the lack of response after nicotine always indicate that there is action on the sympathetic nervous system?

DR. D. RIOCH: This demonstration of reflex activity at Leriche's third level is of considerable physiologic and anatomic interest. I wish to ask Dr. Schwartz

if he would hazard an estimate of the percentage of the total normal response for which this reflex activity at the third level is responsible. Rosenblueth, Brooks and others have been interested in sympathetic reflexes of the spinal cord. Also a number of workers have recently claimed definite autonomic responses from the cerebral cortex. Much of the work published is still unconfirmed, and some of it is questionable. Has Dr. Schwartz any observations bearing on these problems?

Dr. H. G. Schwartz: So far as the action of nicotine is concerned, I was utilizing Langley's own weapons. It was on this basis that he disproved the work of Claude Bernard and François-Franck. In regard to Dr. Rioch's question about the percentage of normal response, it is difficult to hazard a guess. Judging from the degree of response in those animals in which the central connections were preserved, I should say that the reflex through the stellate ganglion probably represents about 15 per cent of the normal response in the forelimb. With regard to the question of Leriche's hypothetic third level, I shall show one slide. I have been doing some work on the higher level, but it is not complete, and I feared to bring it into the body of my report this evening. During the past three months I have been studying the galvanic response in cats with cerebral lesions. I have had interesting results in four animals in which the premotor area was removed. This slide shows the typical results. The galvanic response was abolished on the right (contralateral) side, whereas the usual responses were obtained on the left. The skin of the back was pinched; there was no response on the right and a response on the left. Finally, the tail was pinched; there was no response on the right and a definite response on the left. Pinching the right foreleg produced a response in the right foreleg, i. e., reflex activity through the stellate ganglion. As to why responses to other stimuli were not obtained I am not yet prepared to make a definite statement, but it seems that the premotor area has something to do with it.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 17, 1935

Theodore T. Stone, M.D., *President, Presiding*

Relation of the Hypothalamicohypophyseal System to Diabetes Insipidus. Dr. C. Fisher, Dr. W. R. Ingram and Dr. S. W. Ranson (by invitation).

This paper appeared in full in the July issue of the Archives, p. 124.

DISCUSSION

Dr. Percival Bailey: I have done some work on this subject on dogs. I am persuaded that the theory favored by these authors is not correct, for it is not possible to produce polyuria in this way. An intact anterior lobe of the hypothalamus in the absence of a posterior lobe will not cause polyuria in dogs. The only way in which I have been able to produce permanent polyuria, which I have done in 2 dogs, was to injure the hypothalamus. In my cases removal of the posterior lobe alone did not cause polyuria. The experiments presented by Dr. Ingram show that it is possible to produce polyuria without injuring the posterior lobe. This was shown by my work also, and it has been corroborated by others. It is difficult to conduct cleancut, unequivocal experiments on cats and dogs because of the small size of the region and the complicated relations of the various parts. Monkeys would seem to be better subjects because the hypophysis in them has a relatively long stalk. I undertook some experiments with monkeys, in collaboration with Dr. Van Dyke, but because of his departure for China the results were not published. We found, however, that section of the stalk or placing a clip on the stalk did not produce polyuria in our monkeys.

DR. PAUL C. BUCY: Dr. Bailey did not state that in some of the animals we studied together, both monkeys and dogs, nothing was done except to cut the hypophyseal stalk or to put a silver clip on it. This would interrupt the same fibers which Dr. Ingram interrupted in the hypothalamus and would leave the entire hypophysis intact. In none of these cases did polyuria develop. In the most common clinical cases in which the posterior lobe and the anterior lobe are severely damaged, i. e., in cases of adenoma of the pituitary gland, polyuria rarely develops, whereas cases in which polyuria most commonly develops are those with tumors above the sella turcica, i. e., cases of craniopharyngioma. In these cases the damage to the hypophysis is no greater and may be less than in cases of adenoma, but there is the additional factor of severe damage to the hypothalamus by the supra-sellar tumor. It thus appears from clinical evidence that damage to the hypophysis is not sufficient to produce polyuria, but that rather a hypothalamic lesion is required. The experimental evidence presented here points in the same direction. Lesions in the hypothalamus which included the supra-opticohypophyseal nerve fibers resulted in polyuria; yet destruction of those same nerve fibers by cutting the hypophyseal stalk produced no disturbance in water metabolism. It seems evident from this that destruction of these fibers is not the important factor in the production of polyuria but rather that some other nearby structure in the hypothalamus was damaged by the experimental lesion and that it is the mechanism concerned in this phenomenon.

DR. C. FISHER: In the 2 cats in which the posterior lobe was partially removed no polyuria was observed. Although these animals maintained a normal water exchange under ordinary conditions, it was found that when the antidiuretic mechanism was put under the strain entailed in the attempt to check diuresis they could not respond normally. Thus, when fed salt or thyroid extract, both of which are diuretics, they responded with a much more marked diuresis than did normal cats.

I think that it should be emphasized that the hypothalamus and the posterior and intermediate lobes of the hypophysis must be considered as a unit so far as the regulation of water metabolism is concerned. One cannot speak of diabetes insipidus being caused by an isolated lesion of either the hypothalamus or the posterior lobe. The only hypothalamic lesions which cause permanent polyuria are those which cause atrophy of the posterior lobe as a result of the destruction of the supra-optic nuclei or the fibers which arise from the latter. On the other hand, destruction of the posterior and intermediate lobes results in retrograde degeneration of the supra-optic nuclei. In other words, damage to the supra-opticohypophyseal system at any one of three points, nucleus, fiber tract or posterior and intermediate lobes, will result in permanent polyuria.

After it is demonstrated that the supra-opticohypophyseal system controls the antidiuretic activity of the posterior and intermediate lobes, the rôle which the hypophysis plays in the regulation of water metabolism is by no means completely elucidated. Two important objections have been raised against the theory of the influence of the hormone of the posterior lobe. The first is that although there is good evidence that removal of the posterior lobe will bring about experimental diabetes insipidus (Cushing and Richter) complete removal of the hypophysis does not cause permanent polyuria. The second is that several investigators have been able to elicit transient polyuria in dogs by puncturing the tuber cinereum some time after a previous so-called total hypophysectomy. We believe that if it can be shown that the anterior lobe or pars tuberalis secretes a diuretic substance or substances which in a sense act antagonistically to the antidiuretic hormone of the posterior lobe, these objections will become susceptible of explanation. For example, complete removal of the hypophysis would not cause polyuria because it would mean that two antagonistic principles had been removed, a diuretic and an antidiuretic principle. The second objection is somewhat more difficult to dispose of. However, if it should happen that a remnant of the pars tuberalis or anterior lobe were left after the initial hypophysectomy, such a remnant could easily be irritated during the course of the second operation, when the puncture

is made in the tuber. This irritation might result in transient polyuria. It is, therefore, interesting to note that in 5 of the 7 experiments of this type reported in the literature by Camus and Roussy and by Houssay and Warner the authors themselves noted the presence of remnants of the pars tuberalis or the anterior lobe at autopsy. It should be emphasized that permanent polyuria has never been produced by this double operation, but only transient polyuria.

I wish to give briefly some of the more important evidence in support of the contention that the anterior lobe has a diuretic function. First, Von Hann in 1918 was the first to suggest this possibility on the basis of the examination of a large amount of clinical material he concluded that diabetes insipidus occurs only when the posterior lobe is destroyed and the anterior lobe left intact. Complete destruction of the hypophysis did not cause diabetes insipidus. It is of interest that only six years after the report of the first clinical case of diabetes insipidus definitely said to be of pituitary origin enough clearcut material was at hand to permit Von Hann to advance his theory. Second, our evidence suggests strongly that the transient phase of the polyuria which precedes the permanent phase is due to irritation of the pars anterior or tuberalis. Third, the work with extracts is of importance. At least a half-dozen workers have been able to elicit marked diuresis in the dog and other animals by injecting anterior lobe extracts. Fourth, Richter was able to demonstrate that removal of the posterior lobe of the rat resulted in permanent polyuria, provided sufficient tissue of the anterior lobe was left intact. Richter offered his evidence in support of the Von Hann theory.

There are two theories as to the manner in which the anterior lobe intervenes in water metabolism. The first suggests that there may be a specific diuretic hormone. Barnes, Regan and Bueno, whose work was later confirmed by Biasotti, were able to elicit marked diuresis in dogs by injecting extracts of the anterior lobe. However, such diuresis could not be obtained if the animal had previously undergone thyroidectomy. They concluded that the diuretic activity of the anterior lobe is mediated through the thyroid gland. Following their suggestion we decided to remove the thyroid glands in some of our cats with permanent polyuria, the idea being that the polyuria was due to the diuretic activity of the anterior lobe uncompensated by the antidiuretic effect of the supra-opticohypophyseal mechanism and that if this diuretic activity is carried out through the thyroid removal of the latter ought to cause a cessation of the polyuria. In 3 animals which were thyroidectomized there was a diminution of the polyuria by from one-third to one-half. After a month or more, however, there was an increase to approximately the prethyroidectomy level. Consequently, we conclude that an action through the thyroid is not sufficient to explain the entire diuretic activity of the anterior lobe of the pituitary gland, though this may be one factor.

The second theory, which was advanced by Richter and ourselves, holds that since the anterior lobe controls the level of metabolism, growth, activity, etc., its removal results in a general depression of vital activity and a consequent decreased intake of food and water with a diminished output of urine. In other words, while the posterior lobe antidiuretic hormone acts specifically, the anterior lobe exerts its diuretic effect by its influence on general physiologic processes.

Dr. Bailey states that separation of the stalk alone does not cause polyuria. I wish to emphasize that destruction of the supra-optic tract by placing lesions in the anterior lobe of the hypothalamus, as we have done, is equivalent to separation of the stalk, for the stalk of the pituitary gland is merely the bundle of fibers which arises from the hypothalamus plus a lining of supporting cells.

NARCOLEPSY FOLLOWING HEAD INJURIES. DR. GEORGE W. HALL and DR. GEORGE B. LEROY (by invitation).

EPENDYMOBLASTOMA IN THE FOURTH VENTRICLE WITH NEW BONE FORMATION. DR. ROLAND P. MACKAY.

This article will appear in full in a later issue of the ARCHIVES.

PHILADELPHIA NEUROLOGICAL SOCIETY

Fiftieth Anniversary Meeting, Jan. 25, 1935

THE FIRST FIFTY YEARS OF THE PHILADELPHIA NEUROLOGICAL SOCIETY. DR. WILLIAM G. SPILLER.

The Philadelphia Neurological Society had its origin in the fertile brain of Dr. Charles K. Mills, who called together several physicians in his office in November 1883 to discuss the forming of the society. The transactions of the society begin with the record of the meeting of Dec. 15, 1883. It reads:

"In response to a notice signed by Drs. Mills, Sinkler, Dercum and Eskridge, requesting a meeting of those interested in organizing a Philadelphia Neurological Society, the following named persons met in the Hall of the College of Physicians at 8:30 P. M. of December 15, 1883.

"Drs. Bennett, Avery, Morehouse, Jones, Mills, Kerlin, Reichert, Brubaker, Lloyd, Randolph, Dercum, Given, Sinkler, Brinton, Ott, Angney, Richardson, Chase and Eskridge (19 in all).

"In calling the meeting to order it was moved by Dr. Charles K. Mills and seconded by Dr. Eskridge that Dr. Kerlin act as chairman. The resolution was adopted unanimously. Dr. J. T. Eskridge was appointed secretary.

"At the request of the chair Dr. Mills explained the object of the meeting, and moved that the chair appoint a committee of five on organization to report sometime in January 1884. The resolution was adopted, Drs. Mills, Chase, Eskridge, Brubaker and Sinkler were appointed the committee.

"Drs. Mills, Sinkler, Brubaker and others expressed their views in regard to a Philadelphia Neurological Society.

"On motion the meeting adjourned to meet (convene) at the call of the committee on organization.

J. T. Eskridge, Secty."

A meeting to organize was called for Jan. 28, 1884. The Constitution and By-Laws as presented by the committee were read and adopted. The officers elected were: president, Dr. S. Weir Mitchell; vice presidents, Dr. Charles K. Mills and Dr. Isaac N. Kerlin; secretary and treasurer, Dr. James Hendrie Lloyd; recorder, Dr. Lewis Brinton; councillors, Dr. J. T. Eskridge, Dr. Wharton Sinkler, Dr. S. Preston Jones and Dr. A. P. Brubaker.

No original papers on medical topics were read at this meeting, which has been regarded as the official founding of the society.

Dr. Mills never lost his intense interest in the society, even in his declining days, when, weakened in body and with greatly impaired vision, he was a frequent attendant at its meetings. At every decade until and including that ending in 1924, with the exception of that ending in 1914, he delivered an address on the progress of the society during the previous ten years, making three addresses in all. The decade from 1904 to 1914 was described by Dr. Theodore H. Weisenburg. At that meeting Dr. Mills was president of the society and preferred to give an address on a scientific subject.

At the second meeting of the society on Feb. 25, 1884, Dr. Mills read the first medical paper presented. His title was: "The McGinnis Case." The name of Dr. Bochroch as a member appears in the report of the meeting of Feb. 25, 1884. Dr. Hinsdale was elected to membership on March 24, 1884; he later became secretary and took an active part in the proceedings. Dr. de Schweinitz was elected to membership on Jan. 25, 1886, and is still a member. Dr. S. Weir Mitchell and his staff presented many important cases and papers before the society. Dr. W. W. Keen's first appearance before the society by invitation was on Jan. 26, 1885. He became a member later.

The publication of the Transactions of the Philadelphia Neurological Society in the May 1918 issue of the *Journal of Nervous and Mental Disease* began with the meeting of Feb. 25, 1884, and ended with the meeting of Jan. 25, 1918. At this

time the journal appeared in the form of two volumes a year. During these thirty-four years it was the official organ of the society. I was associate editor of the journal in 1897 and 1898, became full editor in 1899 and remained as such until my resignation with the issue of June 1918, a period of a little over twenty-one years. Dr. Jelliffe has continued as managing editor until the present time.

No reports of the society were published for the period from February to November 1918, inclusive. The ARCHIVES OF NEUROLOGY AND PSYCHIATRY began with the issue of January 1919. It was made the official organ of the society, and the report of the meeting of Dec. 18, 1918, appeared in the issue of February 1919.

In the early meetings of the society a list of the members present was recorded in the minutes of each meeting. There was no difficulty in this as the number was small, but as the society increased in membership it became more difficult to maintain this record, and finally it was inadvisable to do so.

About this period, and a little later, it was not unusual for the members of the council to adjourn to the old University Club on Walnut Street east of Broad Street for a meeting. The site west of Broad Street came later.

Distinguished men were early invited to speak before the society. Dr. L. F. Barker on Jan. 25, 1897, spoke on the subject "The Sense Areas and Associated Centers in the Brain as Described by Flechsig." This was probably the first paper in the English language in which a clear and lengthy presentation of this subject was given. At this time Dr. Barker was associate professor of anatomy in the Johns Hopkins University.

Dr. William Osler, as he was then known, was elected to membership on Jan. 26, 1885. After his change of residence to Baltimore he continued his interest in the society and repeatedly came to attend the meetings, which were always held in the College of Physicians of Philadelphia, at the northeast corner of Locust and Thirteenth Streets. Considerable attention was paid to psychiatry and medicolegal questions at these meetings until, largely under the instigation of Dr. Burr, the Philadelphia Psychiatric Society was formed. Dr. Burr became a member of the Philadelphia Neurological Society on Feb. 27, 1888. Dr. Keen's name as well as those of Dr. J. Chalmers Da Costa and Dr. William J. Taylor appear frequently in the records of these meetings.

Dr. Mitchell remained president for six years. Dr. Mills was nominated for the presidency on Dec. 23, 1889, but he withdrew his name and substituted that of Dr. H. C. Wood, who was clinical professor of nervous diseases at the University of Pennsylvania. Dr. Wood was elected. Dr. Dercum became president on Jan. 25, 1892, Dr. Mills on Jan. 23, 1893, Dr. Sinkler in 1894, Dr. Mills again in 1896 and Dr. Burr in 1897. Thirty-four men have been president. Dr. S. Weir Mitchell served six successive years; Dr. Mills and Dr. Dercum were president three times and Drs. Wood, Burr, Lloyd, Spiller, Potts, McCarthy and Cadwalader each served two terms.

At the meeting of Jan. 22, 1894, Dr. Mills reported on the history and progress of the Philadelphia Neurological Society in the previous ten years, but the published transactions contain no further details.

The meeting of Oct. 25, 1897, was notable because of a paper read by Dr. Thomas H. Montgomery Jr., with the title: "Abstract of Apáthy's Views on the Structure of the Nervous System." It contained a description of the neurofibrils in ganglion cells. One may read that Dr. Alfred Stengel, elected a member on April 25, 1892, in 1897 presented a case of arsenical neuritis, and that Dr. Judson Deland in the same year reported a case of dysphagia. There were presentations of cases or papers by Drs. Rhein, J. K. Mitchell and Eshner and the present dean of the Medical School of the University of Pennsylvania, Dr. William Pepper. The name of Dr. David Riesman, who became a member on Feb. 26, 1894, occurs frequently in many society reports covering a long period; he is still a member.

The meeting of Feb. 28, 1898, was a Johns Hopkins night, possibly in part owing to the association of Dr. Osler; the names of Drs. Simon Flexner, Thayer, Barker and H. M. Thomas appeared on the program. These men, with Dr. Berkley and

Dr. Preston, all of Baltimore, were made active members but were soon placed on the nonresident list. Other distinguished visitors a little later addressed the society; these included Dr. J. J. Putnam and Dr. P. C. Knapp, both of Boston, Dr. M. Allen Starr and Dr. Charles L. Dana, both of New York, and many others. Tumor of the brain was as popular a subject then as now. Tabes in the Negro was regarded as rare, but Dr. J. W. McConnell, who became a member in 1893 and president in 1908, reported 5 cases in Negroes.

The title "Acute Anterior Poliomyelitis Occurring Simultaneously in a Brother and Sister," used for an article by Dr. Frederick A. Packard on Jan. 23, 1899, is interesting because of the early recognition of the transmission of the disease. Dr. Mills remarked that in recent years he had come to the conclusion that anterior poliomyelitis is an infectious disease. Patients with this disease who were in hospital wards were not isolated. Dr. Packard was a trustee of the University of Pennsylvania, and his portrait hangs on the wall of the office of the dean of the Medical School.

Dr. Mellus, of Baltimore, became a member on March 28, 1898, and on several occasions reported the results of his experiments on the brains of apes, especially on the motor tracts. Dr. Lloyd became president in 1899. Dr. McCarthy was elected a member on April 24, 1899. He at once took an active part in the meetings of the society and reported a case of ambulatory automatism at the meeting following his election; later, with Dr. Burr he presented a paper on serous meningitis, another on trophic changes following injury of the supra-orbital nerve, a report on paresthetic meralgia and many others. He became president on Jan. 23, 1906. It is fitting that the society has elected him to be its president in this semicentennial year. Dr. Gordon was elected a member on March 26, 1900, and became president in 1907.

A special meeting of the College of Physicians of Philadelphia was held on April 20, 1900, for the discussion of a paper entitled "The Fifth Pair of Nerves in Its Neurological and Surgical Aspects." The members of the Philadelphia Neurological Society were invited. Dr. Keen was then president of the College of Physicians.

At the meeting of Oct. 22, 1901, Dr. Sailer read a paper on "The Supra-Orbital Reflex." It was discussed by Dr. McCarthy, who had described the reflex. Dr. H. C. Wood resigned as a member at this meeting and became an honorary member at the following meeting. He also resigned about this time the position of clinical professor of nervous diseases at the University of Pennsylvania.

The twentieth anniversary of the founding of the Philadelphia Neurological Society was celebrated on Jan. 26, 1904. The program was as follows:

Dr. Charles K. Mills: Neurology in Philadelphia from 1874 to 1904.

Dr. S. Weir Mitchell: The Evolution of the Rest Treatment.

Dr. James Hendrie Lloyd: The Metaphysical Conception of Insanity.

Dr. J. Chalmers Da Costa: The Surgery of Idiocy and Insanity.

Dr. F. X. Dercum: Mystic Medicine.

The June 1904 issue of the *Journal of Nervous and Mental Disease* was given to the publication of these addresses. The minutes of the society contain their titles and little else, but it is indicated that a banquet was held. No report of the discussion is obtainable. The paper by Dr. Mills was of much historical value, but it embraced far more than a review of the society's activities; it was, as the title indicates, a description of the medical schools and of data of general neurologic interest, such as publications by neurologists which were not presented before the society. Nay, it went much further and

". . . . dipt into the future far as human eye could see; Saw the vision of the world, and all the wonder that would be." Dr. Mills pictured his vision of the centennial of the society in 1984 and described the achievements of neurology by that date. The neurologists then would have a sympathetic compassion for our doings which would bespeak our relative insignificance.

Dr. C. H. Frazier, who was destined to play an important rôle in the society, became a member in March 1905 and president in 1922. Dr. T. B. Holloway became a member on Oct. 21, 1905, and is still a member.

In 1906 it was decided that interurban meetings of the New York Neurological Society and the Philadelphia Neurological Society would be advantageous, and the first meeting of this kind was held in Philadelphia on Nov. 24, 1906, with Dr. McCarthy in the chair. The presentations were by Philadelphia men, and great efforts were made to have the meeting a success. Interesting and unusual cases were shown by Drs. Burr, McConnell, J. K. Mitchell, J. H. W. Rhein, Weisenburg and Gordon and were discussed by the invited guests, including Dr. Fraenkel, of Berne, Switzerland. A paper by me with the title "Psychasthenic Attacks Simulating Epilepsy," with a report of 2 cases, was read. Oppenheim had published a paper a few months previously on this subject. Persons are psychopathic from birth; tics, states of anxiety, phobias and obsessions predominate, and the attack may be a period of unconsciousness or of convulsions. Discussion was given by Dr. Morton Prince, of Boston, who was especially interested in psychopathology; by Dr. Barker, of Baltimore; by Dr. Russell, of Montreal, and by Dr. Dana, of New York. The important discussion on aphasia in a series of papers by Marie and Dejerine had been held earlier in 1906 and had aroused the attention of neurologists everywhere. The subject, therefore, was ripe for this meeting, and the discussion was given by Drs. Mills, Lloyd, Dercum, E. D. Fisher, Starr and Fraenkel.

The members of the Philadelphia Neurological Society visited the New York Neurological Society on March 16, 1907, and on Oct. 22, 1907, an invitation was extended by the Boston Neurological Society to the members of the Philadelphia Neurological Society to meet with them in Boston. The invitation was accepted, and attendance was left to each individual member. The New York Neurological Society repeated the visit to Philadelphia on Dec. 18, 1909. Cases were presented by Drs. Potts, J. K. Mitchell, McCarthy and Dercum. Three papers were read: "The Treatment of Spasticity by Resection of Posterior Spinal Roots" by Dr. Spiller and Dr. Frazier; "Division of the Auditory Nerve for Persistent Vertigo and Tinnitus" by Dr. Frazier, and "Disturbance of Sensation in a Case of Syringomyelia" by Dr. Allen. As in the previous meeting, after the presentation of cases and papers a subject was introduced for discussion. At this meeting "The Clinical Study of Changes in Sensibility Due to Organic and Functional Disease, Especially with Reference to the Methods of Testing" was presented by Dr. Mills, and the discussion was continued by Drs. Starr, Jelliffe and Prince.

Dr. Wharton Sinkler died on March 16, 1910. At the meeting of March 25, 1910, a minute on his death, drawn up by Drs. Dercum, Mills and Lloyd, was read. It was as follows: "The Philadelphia Neurological Society has learned with sincere sorrow of the death of Dr. Wharton Sinkler. Dr. Sinkler was one of the founders of the Philadelphia Neurological Society and a former president; and also one of its most active members. During the twenty-six years of its existence he was closely identified with its work, being an active contributor and always taking a warm interest in its discussions and deliberations. In addition, his personal qualities were such as to endear him to every one of the members of the Society and in his loss we feel that we have been bereft not only of a distinguished scientific collaborator, but also of a friend beloved by all." His portrait hangs on the wall of Mitchell Hall in the College of Physicians of Philadelphia. He was vice president of the college.

The evening of Nov. 27, 1914, was devoted to a scientific meeting in honor of the thirtieth anniversary of the society. The program was as follows:

Dr. Charles K. Mills: Presidential Address: Concerning Cerebral Morphology in Its Relation to Cerebral Localization.

Dr. Francis X. Dercum: Nervous and Mental Diseases and the Newer Pathology.

Dr. James Hendrie Lloyd: The Morphology and Functions of the Corpus Striatum.

Dr. Charles W. Burr: The Psychology of Misers.

Dr. William G. Spiller: Remarks on Central Representation of Sensation.

Dr. Theodore H. Weisenburg: The Founders and Work of the Society.

A dinner was given on the following evening, Nov. 28, 1914. Sixty-six members and invited guests were present. The speakers were: Dr. George W. Jacoby, of New York; Dr. Morton Prince, of Boston; Dr. Hugh T. Patrick, of Chicago, and Dr. Henry M. Thomas, of Baltimore. In addition, remarks were made by Dr. George E. de Schweinitz for the College of Physicians of Philadelphia in the absence of Dr. James C. Wilson, president of the college; by Dr. William Duffield Robinson, president of the Philadelphia County Medical Society, and by Dr. S. D. Risley, president of the Philadelphia Medical Club. Dr. Graeme M. Hammond, of New York, who was for many years secretary of the American Neurological Association, also spoke in response to a call by the president. A letter was received from Dr. William L. Rodman, president-elect of the American Medical Association, expressing his regret that an unexpected call out of the city had prevented him from being present at the dinner as he had expected. In his letter he extended his congratulations to the society, expressing his appreciation of its high position in American medicine.

Dr. Jacoby, in his remarks in behalf of the American Neurological Association, said that that association had been founded in 1875. It elected Dr. S. Weir Mitchell as its first president, but for some occult and never to be disclosed reason he declined to accept the office, and Dr. J. S. Jewell, of Chicago, was elected the standard bearer of the association. Having secured a president, the association determined to retain him, and he was reelected until he had served four years. The list of presidents obtained from Dr. Graeme M. Hammond, secretary of the association, shows that Dr. Jewell occupied the presidential chair five years. The Philadelphia Neurological Society, founded nine years later, was fortunate in securing Dr. Mitchell as president for a period of six years.

Dr. Jacoby said that of the 35 who accepted the invitation to be present on June 2, 3 and 4, 1875, the first meeting of the American Neurological Association, only 20 came, and only 16 names are to be found as original members of the association. How interesting it is to compare this number with the list for 1933-1934 furnished by the present secretary, Dr. Riley, with 43 senior members, 154 active members, 8 associate members and 28 honorary members. It has become unfashionable to decline membership in the American Neurological Association.

Dr. Prince remarked that the original membership of the American Neurological Association was not one of specialists, men who devoted themselves exclusively to neurology; it was in the main rather a membership of internists who had a greater or less interest in neurology. Some of the members had acquired their chief distinction in the practice of general medicine or in other fields. Among these were the well known names of Pepper and H. C. Wood, of Philadelphia. Correspondingly, the papers, with important exceptions, took on rather a clinical and theoretical aspect during the first few years; nor is one impressed with the problems as being of profound significance. Gradually there was an influx of young men who devoted their activities wholly or most intensively to neurology until, about the date of the founding of the Philadelphia Neurological Society, there had arisen a group of thoroughly trained American neurologists, and the great advance in neurology in America was coincident with the founding of this society. The neurologists of that early period were trained to think profoundly; they often forecast the future objective demonstrations of later schools by pure reasoning. Thus Hughlings Jackson may be said to have laid down the principle of cerebral localization on theoretical grounds.

How true this is also of Dr. Mills. His speculations often were based on reasoning, as in his designation of a center for equilibrium or orientation, the representation of the vestibular nerve. The existence of this center has been confirmed by Dr. Spiegel. Other examples could be given.

The *Journal of Nervous and Mental Disease* devoted the June 1915 issue to the proceedings of the thirtieth anniversary of the Philadelphia Neurological Society.

Dr. Isaac Jones was the first to employ the Bárány tests in Philadelphia, and at the meeting on Feb. 26, 1915, he considered this subject before the society.

Drs. Mills, Dercum, Weisenburg and I had recently returned from the International Medical Congress in London in 1913, where we had heard Bárány describe his methods. Dr. Jones wrote an excellent book on the subject and imported all the apparatus used by Bárány. During the World War his services in this work became important, and on his return to this country he moved to California.

At the meeting of April 23, 1915, Dr. Milton J. Greenman, by invitation, presented a paper entitled "Regeneration of Peripheral Nerves." The experiments were made on more than 300 albino rats, and 44 were examined and the results tabulated. Dr. J. E. Sweet applied the results to surgical measures on human beings.

The program for the meeting of April 25, 1919, consisted of a symposium based on the military experiences of members of the society during the recent war. The speakers were Drs. Potts, Price, Woods, Cadwalader, Ingham, Bond, Rhein, McIver, Weisenburg, Leopold, Wilson and Babcock.

At the meeting of Feb. 27, 1920, Dr. Cadwalader reported the case of suture of the spinal cord, done nineteen years previously and reported by Stewart and Harte. This case had received much notice. The separated ends of the severed spinal cord were approximated by sutures only three hours after the injury. No clinical signs of return of function had appeared. This case would seem to have settled finally that regeneration of the spinal cord does not occur after complete section and approximation of the ends by suture. At the meeting of Feb. 7, 1925, Dr. Taft and Dr. Paul described the pathologic changes observed twenty-four years after myelorrhaphy. The essential fact was that in the area of the lesion of the spinal cord no nerve fibers were found.

Dr. C. M. Byrnes, of Baltimore, made many visits to the society and sometimes was accompanied by Dr. A. C. Gillis and Dr. G. Lane Taneyhill, also of Baltimore. Dr. Byrnes was made president on Jan. 26, 1923, and later presented a careful study of the muscle spindles in cases of paralysis agitans.

The celebration of the fortieth anniversary of the foundation of the Philadelphia Neurological Society occurred on Nov. 28, 1924. The meeting was held in Mitchell Hall in the College of Physicians, and the following addresses were given:

Dr. Charles W. Burr: Presidential Address: The Changing Attitude of Psychiatrists Toward Insanity as a Defense for Crime.

Dr. Charles K. Mills: The Work and Workers of the Philadelphia Neurological Society from 1914 to 1924.

Dr. Francis X. Dercum: The Thalamus in the Physiology and Pathology of Mind.

Dr. James Hendrie Lloyd: Trial by Jury.

Dr. William G. Spiller: Rapidly Developing Paraplegia with Carcinoma of Various Parts of the Body.

Dr. Theodore H. Weisenburg: The Weir Mitchell Rest Cure Forty Years Ago and Today.

Twenty honorary members, 13 foreign and corresponding members and 6 associate members were elected.

A dinner celebrating the fortieth anniversary was held at the Art Club in Philadelphia on Nov. 29, 1924, with Dr. Burr as toastmaster. The guests of the evening were Dr. Bernard Sachs, of New York, Dr. Frederick Tilney, of New York, Dr. J. W. Courtney, of Boston, and Dr. Hobart A. Hare, of Philadelphia, president of the society in 1903. Thirty-nine members of the society and 13 guests were present. The names of these as well as of the honorary, foreign and corresponding members and associate members are recorded in the minutes.

The fourth decade was admirably reviewed by Dr. Mills in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY in October 1925 (vol. 14, p. 502). He spoke of the valuable cases which had been presented before the society. This was the period of three great epidemics, poliomyelitis, a virulent form of influenza and epidemic encephalitis. It was also the period of the World War, and Dr. Mills went into details in recording the relation of the society to it; the subject has also been treated by Dr. Weisenburg in the military history of the American Neurological

Association which is to be found in the semicentennial volume of the association. In this volume also is to be found Dr. Jelliffe's excellent presentation on fifty years of American neurology, which covers more than this title indicates.

The meeting of Dec. 20, 1929, was devoted to the celebration of the centenary of the birth of Dr. S. Weir Mitchell, the first president of the society. The papers read were:

Dr. Charles K. Mills: Dr. Mitchell's Services and Writings in the Periods Preceding.

Dr. Francis X. Dercum: Dr. Mitchell, a Physiologist in Research and in Therapeutics.

Dr. James Hendrie Lloyd: The Doctor in Literature.

Dr. Charles W. Burr: Personal Recollections of Dr. Mitchell.

Dr. William G. Spiller: Letters and Reminiscences of Dr. Mitchell.

The saddest duty one can have to perform is to record the passing of four of the most prominent men in the society. Dr. Charles Sower Potts died first. Dr. Mills paid him the following tribute on Feb. 28, 1930. He spoke of Dr. Potts as having been one of the most useful and respected members of the society. He gave a brief résumé of his life and mentioned that he had been president of the Philadelphia Neurological Society in 1904. He had been a constant attendant at the meetings of the society and a frequent contributor to its proceedings.

The remaining three men were Drs. Dercum, Mills and Lloyd. All were founders of the society. Dr. Brubaker is the only one of the founders who is still living. Dr. Dercum died on April 23, 1931. Dr. Mills paid him the following tribute: "Dr. Dercum was one of the most prominent men in the society. He was a disciple of Darwin and his school of evolutionists. He did excellent work both at the Academy of Natural Sciences and in the University of Pennsylvania. Some of this work was under the stimulus and supervision of Dr. Joseph Leidy. His last appearance before the community had about it an heroic aspect. He fought his last battle for science with his back to the wall and his sword in hand." In explanation of this statement it may be added: Dr. Dercum knew he had cardiac weakness and that physical and mental strain were dangerous; nevertheless, on April 23, 1931, he made his presidential address before the American Philosophical Society and at its close sat down, his head fell forward and life had passed.

Dr. Mills died on May 28, 1931.

Resolutions on the death of Dr. Mills, read by Dr. Lloyd on Oct. 23, 1931, are: "Resolved, that the Philadelphia Neurological Society herewith records its deep sense of loss in the death of Dr. Charles K. Mills on May 28, 1931 in his 86th year.

"That the society here commemorates the services of the member who was first to suggest its organization, and was one of its founders in 1883, nearly one half a century ago.

"That in the long career of Dr. Mills it recognizes the work of a devoted scientist, who contributed to the progress of neurology in all its branches, and who not only won wide recognition for himself, but also reflected honor upon his fellows of this society. His literary works are a legacy which he leaves to his profession.

"That as a psychiatrist Dr. Mills also won distinction as a conservative thinker who was not swayed by mere novelties, but adhered to a time-honored system of mental disorders, as shown especially in his medico-legal work in the courts. The medical jurisprudence of insanity, as understood in his day, owed not a little to his firm and courageous stand in cases of the criminal insane.

"That in the character as in the professional attainments of Dr. Mills the members of this society have long recognized the qualities of the highest type of the physician and the man; and that in his passing they lost both an inspiring colleague and a valued friend."

On March 18, 1932, a memorial meeting was held in honor of Dr. Mills. The program was as follows:

Dr. Charles H. Frazier: Dr. Mills' Interest in Neurosurgery.

Dr. William G. Spiller: Dr. Mills as a Neurologist.

Dr. Charles W. Burr: Dr. Mills as a Teacher of Mental Diseases.

Dr. J. W. McConnell: Personal Associations with Dr. Mills.

Dr. Williams B. Cadwalader: Dr. Mills and Dr. S. Weir Mitchell.

Dr. Theodore H. Weisenburg: Dr. Mills and the American Neurological Association.

Dr. Lloyd died on March 14, 1932. In the resolution on his death by Dr. Burr and Dr. Ludlum, Dr. Lloyd's early life was mentioned briefly, and this tribute so justly deserved was paid:

"Dr. Lloyd was one of the most intellectual men in the medical profession and had wide cultural interests. He had what is so rare, the ability to present his material in such an arresting and interesting manner that his audience at once felt not only his personal charm, but at the same time was made aware of the wide grasp of his knowledge of the subject. His life should be an inspiration to the younger man for in spite of the fact that he was handicapped most of his life by loss of hearing he never lost courage but kept on fighting with undiminished zeal to the end."

At the meeting of Jan. 27, 1933, resolutions were presented by Dr. Ornsteen and Dr. Myers on the death of Dr. Max Henley Bochroch. His early life, hospital associations, official positions and society memberships were mentioned. The following tribute was given: "Dr. Bochroch died November 27, 1932, from a cardiac ailment. Max Bochroch's charm and personality will not be forgotten by those who knew him intimately, nor will his strikingly colorful appearance leave the minds of those who had not known him personally.

"The Philadelphia Neurological Society regrets his passing and expresses its sympathy to his widow and daughter."

The society met with a severe loss in the death of Dr. Theodore H. Weisenburg on Aug. 3, 1934. He had been a frequent attendant at the meetings of the society from the date of his election to membership, Nov. 25, 1902, until the late years of his life, and had been its president in 1909. His memory will be kept alive largely by his editorship of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY from its foundation to the date of his death. This journal had doubled in size and importance as the years passed. Dr. Weisenburg will be remembered for his recognition of neuralgia of the glossopharyngeal nerve, and for the first Charles K. Mills lecture. One obituary was written by his friend, Dr. Frederick Tilney, who well performed the task; another was written by Dr. J. W. McConnell, who knew him intimately and gave a succinct and just appreciation.

In addition to giving a historical review of the society, it seemed at first desirable to mention by name and title of presentation those members who have been especially conspicuous by the excellence of their work during the period considered, and indeed a lengthy list has been arranged; but as the work of preparing this address progressed it became apparent that any such attempt must be regarded as inadvisable, considering the limited period for delivery allotted to me. Dr. Frazier has been able to devote more time to this aspect of the subject and to mention more members of the society by name.

The custom originated by Dr. Frazier in 1923 of devoting one meeting of the society yearly to the consideration of neurosurgical problems has been continued to the present time. As shown in the programs of these meetings, he and the staff under his direction have presented many papers of much value, and this recognition should be included in the historical review of the society.

The neurologic department of the University of Pennsylvania is deeply indebted to Dr. Pancoast, Dr. Pendergrass and their staff, and it is a pleasure to mention the honor shown to Dr. Pendergrass and Dr. Fay in 1929, when the gold medal of the American Medical Association for the scientific exhibit was awarded to them for their work in encephalography.

Acknowledgment is due Dr. Holloway and his staff. The accurate fields of vision taken in his laboratory of perimetry by Dr. Hazel Wentworth have assisted greatly in the diagnosis of intracranial lesions.

FIFTY YEARS OF NEUROSURGERY. DR. CHARLES H. FRAZIER.

In reviewing the history of the Philadelphia Neurological Society as it relates to surgery, this half-century may be divided into two periods, the period before and the period after the advent of the neurosurgeon. In the former, surgical procedures were primitive and had to do mostly with the peripheral nerves and the effects of trauma. In the latter period the neurosurgeon has found himself absorbed almost wholly with the problem of tumors—tumors of the spinal cord, but preeminently tumors of the brain. For all time it would seem that tumors of the brain will be the major interest of the neurosurgeon.

Alas, the Philadelphia Neurological Foot-Ball Team, to which Dr. H. M. Thomas referred at the time of the twentieth anniversary, has been sadly depleted. He said: "There are nerve doctors and other doctors and ordinary nerve doctors and nerve doctors Philadelphia style and what a team you are, with Mills, center, Dercum and Lloyd guards, Burr and Weisenburg, tackles, Keen and Frazier at the ends, with Spiller giving the signals at quarter and John K. Mitchell, McCarthy and Allen in the back field."

I shall refer to contributions in the following order: the peripheral and cranial nerves, spasmodic torticollis, major neuralgia of the trigeminal nerve, the sympathetic system, the spine and spinal cord, the cerebrospinal fluid, trauma of the brain, epilepsy, the hypophysis and abscess and tumor of the brain.

Peripheral Nerves.—Throughout this half-century clinicians and surgeons alike have been battling with sciatica. So far as surgical procedures are concerned, no panacea has been found. In 1889 Dr. S. Solis-Cohen claimed to have obtained a cure in an obstinate case of sciatica by deep injections of osmic acid after he had failed to get results by nerve stretching, then and for many years a popular though not appealing mode of attack. In 1890 Dr. Mills spoke to the society on 2 cases of sciatica in which the patients were operated on by Dr. Deaver. Dr. William J. Taylor has recently presented again his surgical treatment for sciatica before the society. In quite recent times I ventured to perform unilateral cordotomy, but the propriety of such an ordeal may be questioned despite the fact that one is dealing with a lesion which is in some cases distressing and crippling.

Here and there is an occasional title on the society's programs that has to do with the peripheral nerves. Dr. Wharton Sinkler presented a paper in 1895 on suture of the nerves; in 1901 Dr. W. W. Keen reported complete reestablishment of function after secondary suture of the posterior interosseous nerve, and in 1923, Dr. F. C. Grant presented a specimen of sarcoma from the median nerve.

During the World War, the opportunities for dealing with traumatic lesions of the peripheral nerves were abundant. Apparently this subject was brought to the attention of the society at one of its meetings, but in May 1919 the society was the guest of the staff of the United States General Hospital No. 11, and for its entertainment an elaborate program was prepared which illustrated the effects of gunshot wounds of the peripheral nerves, the head and the spine. At the next regular meeting the society adopted the following resolutions:

"I move that the Philadelphia Neurological Society express grateful appreciation for the opportunity which has been afforded by the Staff of this Hospital to investigate, study and see the results of the great work done here.

"I move also, that a minute be made at this meeting which shall include the program presented here, and

"Thirdly, that those who have presented communications and exhibited cases shall be requested to send brief abstracts to Dr. George Wilson, Editor of the Transactions of the Philadelphia Neurological Society in order that these abstracts may be published in the ARCHIVES OF NEUROLOGY AND PHYCHIATRY.

In passing, mention might be made of a discussion in February 1913 of brachial paralysis in children, or birth palsies, by Dr. T. Turner Thomas, a subject in which he has particular interest and to which he has made many valuable contributions. In 1911 I reviewed in extenso my experience and that of others with injuries of the brachial plexus in adults (*J. A. M. A.* **57**:1957 [Dec. 16] 1911).

Cranial Nerves.—The cranial nerves, at least some of them, have retained the attention of neurologists and neurosurgeons for a number of years. So far as they present lesions which at times may with propriety be corrected by surgical measures, I may refer to the fifth, seventh, eighth, ninth and twelfth cranial nerves.

At none of the meetings of the society in these fifty years has neuralgia of the glossopharyngeal nerve been discussed, although by some it is regarded as being as definite a clinical syndrome as tic douloureux. On one occasion my associate Dr. Grant sectioned the glossopharyngeal nerve to bring about relief from pain, and on one occasion (April 1926) Dr. Fay presented a case in which he sectioned this nerve and the posterior cervical roots to give relief from pain in the throat in a case of carcinoma.

In the early days of neurosurgery Dr. Mills offered many suggestions as to the application of surgical procedures to neurologic problems. He was a leader and pioneer in every sense of the word, and at the December 1909 joint meeting of the Philadelphia Neurological Society and the New York Neurological Society, I presented a case in which, at the direction of Dr. Mills, I had sectioned the auditory nerve for persistent tinnitus. Whether Dr. Mills regarded this case as one of Ménière's disease I have forgotten, but many years later Dr. Dandy proposed the same operation in treating persons with true Ménière's disease, and in 1932 Dr. Grant presented a patient in whom the symptoms had been relieved by this procedure. Since that time the operation has been accepted in the neurosurgical clinic of the University of Pennsylvania as a justified undertaking.

Anastomosing operations for facial paralysis are, of course, an old story, but facial tic or facial spasm has been accepted as a bugbear. Dr. Spiller, in 1908, spoke of the effect of injections of alcohol for its relief, and in October 1929 I reported my experiences with an operation proposed by a former assistant, Dr. Ward Williams, which consisted in resecting those branches of the facial nerve which supply the corrugator supercilii and the orbicularis palpebrarum muscle. This operation has been repeated with only a measure of success in cases of blepharospasm.

Ten years ago, for the first time, the possibility of dealing with bilateral paralysis of the recurrent laryngeal nerve by nerve anastomosis was considered. The problem at first seemed analogous to that of facial paralysis, but later it proved to be much more complicated. At all events, in over 20 cases anastomosis was effected between the descending hypoglossal nerve and the paralyzed recurrent laryngeal nerve. Complete restoration of function was obtained only once. In the other instances voluntary movements were restored, as in talking, but not involuntary movement of the vocal cords, as in breathing. The physiologic principle involved in this difference between the restoration of voluntary and that of involuntary movement is still a mystery.

Spasmodic Torticollis.—In the early days spasmodic torticollis claimed the attention of neurologists and surgeons alike. In 1888 Dr. Dercum presented to the society the records of cases of what he called "rotary spasm," or spinal accessory spasm, in a number of which cure had been effected by resection of the spinal accessory nerve. Incidentally, he stated that Dr. H. C. Wood had successfully treated a patient by severely cauterizing the back of the neck with a hot iron. Dr. Dercum took this cue from Dr. Wood, but without effect. The question arose in the discussion as to whether the condition was of spinal or of cerebral origin, and whether the lesions were cortical or deepseated. Dr. Dercum realized that in addition to the trapezius and the sternocleidomastoid muscles, supplied by the spinal accessory nerve, 9 other muscles were involved in the act of turning the head and neck.

In a discussion on rotary spasm (*J. Nerv. & Ment. Dis.* **17**:427, 1890) Dr. S. Weir Mitchell said that he was the first to use gelsemium, in some cases with complete cure. In the same year Dr. Deaver described at great length what he called "ligature of the spinal accessory nerve." Dr. W. W. Keen questioned at one time whether cortical excision should be done in cases of spasmodic torticollis, but soon afterward (Oct. 27, 1890) he described what was the first intelligent

contribution to the surgical treatment of this distressing condition (*Ann. Surg.* **13**:44 [Jan.] 1891). The operation involved resection of the first three cervical nerves after their emergence from the spinal foramina. It was not easy of performance; in fact it was, as I can testify, an extremely tedious procedure. I performed the operation a number of times, but never, as I recall, with complete recovery.

Since that time, forty-four years ago, the neurosurgeon (Spasmodic Torticollis: Interruption of Afferent System Alone in the Treatment, *Ann. Surg.* **91**:848 [June] 1930), on the basis of various hypotheses, has been dividing the roots of the upper cervical nerves within the spinal canal, sometimes the posterior roots of the first, second and third cervical nerves and sometimes the anterior and posterior roots, sometimes on one and sometimes on both sides. However, the problem is still unsolved. There is no accepted surgical method that gives assurance of complete relief. There is improvement, yes in many cases, but absolute cessation of the spasm in few. And as to the etiology, whether wholly functional or organic, striatal or of other origin, no one dares speak without fear of controversy.

Major Neuralgia of the Trigeminal Nerve.—This condition has always been a subject of great interest to this society. Through the efforts of Dr. Spiller the accepted present surgical treatment was evolved. His suggestion in 1898 of sectioning the sensory root behind the ganglion has greatly simplified the operative treatment, with consequent reduction of mortality to less than 1 per cent. There are few operative procedures more certain to bring immediate relief than this.

As far back as 1886 and 1887 two papers were presented to the society on this subject, the first by Dr. Hinsdale and the second by Dr. Dercum. The titles and content of these two articles illustrate well the methods of treatment then proposed. The title of Dr. Hinsdale's paper was "Facial Spasm and Tic Douloureux with Neurectomy and Neurotension." Dr. Dercum reported on "A Case of Tic Douloureux of Twelve Years' Standing Which Has Been Benefited by Large Doses of Salicylates." Surgery in 1886 had not reached the stage at which intracranial operations which included the opening of the subarachnoid space could be performed with safety. Hence, neurectomy of peripheral nerves or avulsions of nerve trunks were all that good surgical judgment advised. As Dr. Dercum's title indicated, even these minor operations were not often advised, and drug therapy was the usual resort in attempts to establish relief from this pain.

Curiously enough, apparently twenty years passed before this subject received further attention before this society. In this period, of course, tremendous surgical progress had been made. No longer were surgeons fearful of opening the skull. In England, Macewen, Godlee and Horsley, in Germany, Krause, and in this country, Keen, Cushing and Frazier had successfully removed intracranial tumors, excised the gasserian ganglion and finally learned to section the posterior root behind the ganglion. But it was not to report surgical experiences that in April 1906 Dr. Spiller described 2 cases of neuralgia of the trigeminal nerve in which operation brought about relief. Rather he emphasized the fact that while the face on the side on which operation was performed was completely anesthetic to touch and to temperature, nevertheless the sensation of deep pressure was in part, at least, preserved. He predicted, therefore, that sensation of deep pressure in the face was subserved by the facial nerve, hitherto supposed to be entirely motor in its function. At the same meeting Dr. Spiller also reported 2 cases before the society in which sensation of deep pressure was preserved after removal of the gasserian ganglion for tumor of the ganglion, and in one of these the sensory root of the fifth nerve was also divided behind the tumor. No similar observation antedating Dr. Spiller's had hitherto been made. In lecturing to the students of the University of Pennsylvania School of Medicine in 1907, he suggested that one or two of them might make this observation the subject of study; in this way, the paper by Ivy and Johnson was written and published in the *University of Pennsylvania Medical Bulletin* in May 1907. They confirmed Dr. Spiller's observation that pressure sense was retained, although all other forms of sensation were lost. In 1911 Dr. Woods described the segmental distribution of the trigeminal nerve.

Nonsurgical methods for the relief of neuralgia of the trigeminal nerve were described in 1911 by Dr. Patrick, who detailed the technic for injection of alcohol into the three divisions of the trigeminal nerve at their point of emergence from the skull. In 1913 Dr. Byrnes and in 1916 Dr. Dorrance outlined their results in the treatment of persons with neuralgia of the trigeminal nerve by direct injection into the gasserian ganglion following the technic described by Härtel in Germany.

The importance of careful differentiation between major and minor facial neuralgia was emphasized by Dr. Burns in 1916. He described the case of a patient who had had 4 operations directed against the trigeminal nerve, including removal of the gasserian ganglion, without relief from pain. In 1920 Dr. Woods again called attention to this fact by exhibiting a patient presumed to have major neuralgia of the trigeminal nerve whose pain had not been in any way affected by section of the posterior root behind the ganglion. In 1917 one of the first cases of tumor of the gasserian ganglion in which the diagnosis was made preoperatively and successful removal carried out was described before this society by Dr. Frazier.

One of the great drawbacks to complete section of the root of the trigeminal nerve is the possibility of keratitis in the ipsilateral eye. In May 1924 Dr. Russel presented a patient on whom a refinement in operative technic had been practiced. Only the outer two thirds of the posterior root had been sectioned, leaving intact the inner third, supplying the supra-orbital branch and the cornea. In this way corneal anesthesia was avoided and keratitis prevented.

Not only the pain of major neuralgia of the trigeminal nerve but also the pain due to malignant disease in the face and neck and the pain of so-called atypical facial neuralgia, or minor neuralgia, was of interest to this group. Dr. Temple Fay was particularly interested in these subjects. In 1926, 1927, 1928 and 1929 he presented papers describing a method for the relief from pain due to cancer of the throat by a combined section of the fifth and ninth nerves by a cerebellar approach. In three subsequent papers he detailed at length the clinical peculiarities distinguishing the pain of minor, or atypical, neuralgia and made definite suggestions for relief. In 1929 Dr. Gotten described a second case in which both the fifth and the ninth nerves had been sectioned through the posterior fossa to give relief from pain.

In 1932 Dr. Spiller summed up clearly on the basis of his long clinical experience the anatomic and clinical basis for the subtotal resection of the sensory root of the trigeminal nerve for obtaining relief from tic douloureux. He stated that whether or not one accepts the fact that the sensory fibers change their relative positions in the root in passing backward from the ganglion to the pons, so that the outer two thirds of the root may not contain all the fibers from the second and third divisions, nevertheless the anesthetic area in the face produced by subtotal section of the root is extraordinarily uniform. He rather doubted the anatomic and histologic evidence brought forward to support the claim that the fibers change their relative positions and shift back and forward in the root. He stated the belief that since sensory studies of the anesthesia produced by excision of the outer two thirds of the root near the ganglion had definitely included only those areas of skin known to be supplied by the second and third divisions and because the anesthesia in these areas had always been so complete, he would have no hesitation in advising this method for securing relief from pain.

Sympathetic System.—Curiously enough, the medical profession of Philadelphia and the environs have paid scant attention to the tremendous interest elsewhere in surgical procedures on the sympathetic system. Perhaps this sweeping indictment does not apply to the members of this society, since many of the conditions for the relief of which operation on the sympathetic system has been undertaken are of vascular origin. Thus, angina pectoris, hypertension, Buerger's or Raynaud's disease, intermittent claudication and retinitis pigmentosa, not to speak of other lesions, all have responded to interruption of sympathetic impulses.

Speaking of Raynaud's disease, Dr. William Osler presented in January 1888 what he called "local asphyxia of the fingers," which seems akin to the picture of what Raynaud described. In January 1921 Dr. G. P. Muller presented a patient

with this disease whose condition improved following brachial sympathectomy, and in 1932 I related to the society my experience of an unsuccessful attempt to combat the pain of atypical neuralgia by removal of the superior cervical ganglion. In every instance, and there were 10 cases, the operation was a failure (Atypical Neuralgia: Unsuccessful Attempts to Relieve Patients by Operations on the Cervical Sympathetic System, ARCH. NEUROL. & PSYCHIAT. **19**:650 [April] 1928).

In the preface to a clinical report (1932) which included the effect of sympathectomy in cases of Raynaud's and Buerger's disease, scleroderma, atypical neuralgia, retinitis pigmentosa, Volkmann's paralysis and chronic arthritis—what a miscellaneous and apparently unrelated group—I forecast the expansion of surgical measures on the sympathetic system pari passu with a more exact and intimate knowledge of the anatomy of the sympathetic system. In all of the lesions, save two, scleroderma and atypical neuralgia, my experience with the operation had been one of great satisfaction as measured by the relief to the patient. Fortunately, surgical procedure on the sympathetic system has not fallen into the discard elsewhere. It has a large sphere of usefulness, and with such leaders as Adson blazing the trail it will soon be found that sympathectomy will be a recognized and conventional procedure in not a few lesions for the relief of which no other remedy exists.

Spine and Spinal Cord.—Spinal Trauma: In considering surgical procedures on the spine and spinal cord one must include spinal trauma and tumors of the spinal cord, traumatic lesions, rhizotomy and chordotomy. I never think of trauma of the spinal cord without a vivid recollection of that brilliant research by that unusual personality Dr. Alfred Reginald Allen. No doubt the record of his accomplishments will be mentioned by others at this anniversary meeting but I should feel remiss did I not refer to his labors as they pertain to a subject of great interest to the neurosurgeon. All will remember the title of his contribution, "The Surgery of Experimental Lesions of the Spinal Cord Equivalent to Crush Injury of Fracture Dislocation of the Spinal Column," and how by an immediate median chordotomy in the swollen edematous cord at the experimental lesion he was able to preserve function under circumstances which otherwise inevitably would have resulted in a complete and permanent transverse lesion. It was a brilliant contribution conceived by a mind always restless and fertile.

In November 1902 Dr. Spiller (*Univ. Pennsylvania Med. Bull.* **15**:483, 1902-1903) described in his customary painstaking way the effect of traumatic lesions of the spinal cord without fracture of the vertebra. Did time and space permit I should like to review this important contribution. It is replete with information as to the effects of trauma of the spinal cord with which the neurosurgeon should be familiar. And, speaking of trauma of the spinal cord, mention should be made of the report (December 1904) by Dr. Charles S. Potts of a case of traumatic hematomyelia. Dr. William Osler, during his residence in Philadelphia, made a number of interesting presentations to this society on various subjects, and in this connection I am reminded of his presentation of a case of trauma of the cauda equina.

Tumors of the Spinal Cord: The first operation for the removal of a tumor of the spinal cord reported to the society will be found in the *Journal of Nervous and Mental Disease* (**16**:228, 1889). In his introduction to the operative report, Dr. Deaver stated that the patient, having been etherized, was placed on the table, and with Prof. D. Hayes Agnew and Prof. John Ashhurst Jr. assisting and in the presence of Dr. J. Hendrie Lloyd and Dr. Charles K. Mills, the operator made a longitudinal incision, etc. Presumably the case was one of a tumor of a cervical vertebra and not of the cord itself. There was some question whether the patient's death might not have been due to injury of the cord in the neighborhood of the phrenic center with an exploring needle. The author, in commenting on the loss of his patient, said that "in future, if I have the opportunity to operate on the cervical portion of the spinal cord, I certainly will not use the exploring needle as a means of diagnosis, but will depend upon exploration and inspection."

Tumors of the spinal cord have received scant attention on the programs of the Philadelphia Neurological Society. To be sure, the tumor of the spinal cord as a neurologic problem is not as absorbing as that of tumor of the brain, and tumors of the spinal cord are relatively infrequent. Then, too, from the standpoint of the neurosurgeon the technical problems in the removal of these tumors are comparatively simple, and with the aid of injections of iodized oil segmental localization has been reduced to an easy interpretation of the x-ray film. But in this historic sketch I should be remiss did I not refer to the first contribution in the proceedings of the society on spinal tumors, a paper by Dr. Mills (November 1885) which deals particularly with the diagnosis and contains much that today, fifty years later, will prove helpful to the student and practitioner alike.

It is interesting to note that in Dr. Mills' discussion of the diagnosis of tumors of the spinal cord he prefaced his remarks by saying that such tumors are of constitutional or of specific origin, such as syphilis, tuberculosis, cancer, etc. This was in 1886, when of course little was known of the different types of tumors of the spinal cord.

Apart from the introduction of iodized oil as a means of localization, the only contribution with claims to originality was presented to the society by Dr. Temple Fay at its May meeting in 1927. He demonstrated, from a series of 13 verified cases, the localizing value of vasomotor and pilomotor manifestations. He claimed that the vasomotor line of demarcation proved to be the most reliable sign and determined in each case the exact level of the lesion. For the neurosurgeon, the vasomotor level indicates the root level and determines the precise site for exploration. The line of sensory loss may be at a lower level.

Sundry contributions dealing with tumors of the spinal cord have been brought to the attention of the society, such as those of Dr. Frazier (February 1921), Dr. Spiller (January 1923), Dr. Weisenburg and Dr. Grant (1928), Dr. Grant (November 1932), who referred to a tumor of the cervical portion of the spinal cord without sensory symptoms and gave a statistical study of 39 fibroblastomas, and Dr. Frazier (April 1933). These papers deal exclusively with the operable tumors, the fibroma or the fibroblastoma.

Somewhat out of the usual run of lesions of the spinal cord is telangiectasis. It is not of common occurrence and may be present for many years without producing symptoms. Two examples of this condition have been under observation in the neurosurgical clinic. One case was that of a woman, aged 25; the history and operative data were presented to the society by Dr. Spiller (with me) in January 1928. The second case was that of a man, aged 50. This case was described by Dr. E. C. Russel (with me), and the paper was subsequently published in a foreign journal (*Arch. franco-belges de chir.* **28**:140 [Feb.] 1925).

Although circumscribed serous spinal meningitis had been discussed by Schlesinger in 1898, in this country one always thinks of Spiller. It was he who reported the first case in this country in 1903 in the columns of the *University of Pennsylvania Medical Bulletin*, and in 1910 Dr. Weisenburg, with Dr. Muller, discussed at some length the etiology and pathology and included in the paper the report of a case in which the patient was relieved by operation. Essentially the lesion seems to be an arachnitis and corresponds in its physical make-up to what in the brain is called pseudotumor.

Suture of the Spinal Cord: All the members remember the case which aroused so much discussion when Stewart and Harte (*Philadelphia M. J.* **9**:1016 [June 7] 1902) announced partial return of function after suture of the spinal cord. The cord was partially severed by a gunshot wound. When the patient died twenty-four years later, Dr. Taft and Dr. Paul (February 1925) demonstrated the cord to the society. In the discussion Dr. Cadwalader said that the patient exhibited all the signs of a transection of the cord. In reading this report I was reminded of an equally famous case, likewise unfounded, in which a distinguished member of the American Surgical Association maintained that after the implant of a graft of the sciatic nerve to repair a defect in the damaged cord the patient had recovered some function.

Chordotomy: Second only in importance to his contribution to the surgical treatment of major neuralgia of the trigeminal nerve in 1899, purposeful section of the sensory root, was Dr. Spiller's proposal in 1912 that the anterolateral columns of the cord be cut to give relief from pain. Though the operation had been performed in the neurosurgical clinic a number of times, the subject was brought first to the attention of the society in March 1917 by me in a paper on chordotomy for relief from pain (ARCH. NEUROL. & PSYCHIAT. **4**:137 [Aug.] 1920). The technic of the operation has been modified and in many ways improved since first practiced, and while it is appropriate particularly in cases of intractable pain accompanying inoperable carcinoma of the pelvis and spinal column, it has been applied to advantage in a wider field, as in cases of painful stumps, stubborn cases of sciatica and cases of Hunner's ulcer, and is, so far as I know, the only measure by which relief from pain may be effected in stubborn cases of herpetic neuralgia. Though proposed twenty-three years ago, the real usefulness of the operation still is not appreciated by the medical profession at large. I regard this operation as one of the greatest surgical triumphs as a means of securing relief from unbearable and ever-increasing pain. More recently, other methods for giving relief from pain have been introduced, for example, intradural injections of alcohol and resection of the presacral nerve, but neither of these methods will ever take the place of chordotomy. Chordotomy will remain an accepted procedure when widespread pain has exceeded the bounds of human toleration. And anent the subject of chordotomy, I wish to include reference to Dr. Temple Fay's observations (April 1926) on the effect of the operation on spasticity and the reactions of defense.

Rhizotomy: Section of the posterior roots of the spinal cord has been applied for giving relief from pain in a number of cases, but only with a modicum of success. In a paper read before the society in May 1918 (Frazier) a series of cases were reported in which this operation had been performed to secure relief from pain in cases of gastric crisis, metastatic carcinoma of the spine, herpetic neuralgia and neuralgia of the brachial plexus. The results were not brilliant. Compared with chordotomy, rhizotomy has no advantage. As from five to seven roots must be cut, a more extensive laminectomy must be performed, and there is always the uncertainty as to how many roots should be cut. Perhaps the only indication for the operation as a relief measure is in cases of neuralgia of the head accompanying malignant invasion of the cervical lymph nodes; both Dr. Grant and Dr. Fay have recorded their experience with this procedure. But section of the posterior roots of the spinal cord has been practiced to combat conditions other than pain. In a paper read before the New York Neurological Society on March 7, 1905, Dr. Spiller advocated the operation for relief from spasticity in the following words: "Where athetosis exists, the muscles are in a state of great tonicity and often are abnormally well developed and abnormally strong. Theoretically, the proper procedure might be to cut posterior roots of the affected limbs, the number to be cut depending on the condition in each case; but this is always a serious operation, and the results have at times been unexpectedly grave."

However, it was not until 1909 that Dr. Spiller's recommendation was put into effect, and the results of the operation were presented on Dec. 18, 1909 at a joint meeting of the Philadelphia Neurological Society and the New York Neurological Society. My associates and I have practiced the operation in a number of cases since then, mostly on children. But while the results were far from brilliant, this means of dealing with spasticity seems, I think, unjustly to have fallen into the discard. The difficulty in the presence of intense spasticity of determining how much residual power may be present embarrassed us in the selection of cases. I still believe that the operation is founded on sound physiologic principles, since it is generally accepted that the dorsal roots control muscle tonus, and has a place in properly selected cases.

In June 1930 the attention of the society was called (Frazier) to the usefulness of this operation in treatment of spasmodic torticollis.

Spina Bifida: All are familiar with the accepted technic for the radical cure of spina bifida. At the May meeting in 1934, Dr. G. M. Dorrance proposed repeated drainage of the sac, especially for patients who presented a bad surgical risk and particularly when the granulated surface had not become epithelized. After repeated tappings the wall of the sac becomes thickened, and the epithelial proliferation proceeds more rapidly.

Cerebrospinal Fluid.—Problems relating to the physiology of the cerebrospinal fluid have attracted wide attention, particularly in recent years and especially by the activities of the younger neurologists in Boston. However, in this review of the activities of the Philadelphia Neurological Society mention might be made of the contributions of some of its members. In 1914 the chairman's address before the Section on Surgery at the June meeting of the American Medical Association was devoted to the cerebrospinal fluid as a problem in intracranial surgery. In the same year and in the year following, Dr. C. H. Frazier and Dr. Max Peet (*Am. J. Physiol.* **36**:464, 1915) engaged in some interesting experiments that had to do chiefly with the production of cerebrospinal fluid, and while subsequent investigations in other laboratories have not borne out the conclusions at which they had tentatively arrived, at the same time the conclusions were interesting. Of all the organ extracts which were used, including pancreas, spleen, kidney, liver, etc., the thyroid gland was the only one which seemed to have a specific inhibitory effect on the activity of the choroid plexus, independently of the condition of the blood pressure. This work was followed up with a study on the influence of di-iodotyrosine and iodothyrine on the secretion of the cerebrospinal fluid (*Am. J. Physiol.* **38**:93, 1915), and at another time they reported the result of studies on the channels and factors influencing absorption of the fluid (*Am. J. Physiol.* **35**:268, 1914).

Clinical methods of measuring cerebrospinal fluid pressure have been recognized as crude. Certainly they are not acceptable to the physiologist, with his technic of precision. To meet these objections, Drs. Lewis, Duane and Ravdin, in Dr. Ravdin's laboratory of surgical research, perfected an apparatus with which pressure could be recorded by the closed method. It was of especial value in that comparative readings of pressure could be made with the experimental animal in any position. Their apparatus has been accepted by physiologists generally and used for the measurement of pressure in other cavities of the body.

Injection of Air: Ventriculography and Encephalography: In 1919 and 1920 Dr. Dandy made the bold, original suggestion that the size, shape and position of the cerebral ventricles and subarachnoid cisternae and sulci could be demonstrated roentgenographically by removing the cerebrospinal fluid and replacing it with air. He further claimed that by changes in the position and contour of the ventricular system the position of any intracranial mass lesion could be determined. This method of diagnosis and localization of tumors of the brain has been of vital importance to neurosurgery. Coincidentally, Bingel, of Germany, proposed the injection of air by the spinal route (encephalogram).

At this time advances in surgical technic had made possible the exposure of any part of the brain with relative safety. But purely neurologic methods of diagnosis were woefully inaccurate. Not more than 60 per cent of intracranial tumors could be localized by these means. It was the day of the exploratory craniotomy and the palliative subtemporal decompression, of improperly placed osteoplastic flaps, of tight brains and of inadequate understanding of how to control increased intracranial pressure by ventricular tap or hypertonic solution. Only too often, after the most careful evaluation of the available neurologic evidence, no tumor would be revealed by exploration, the extreme intracranial tension would result in cerebral herniation to such an extent that sacrifice of the bone flap became necessary, and subsequently the skin sutures would give way before the persistent pressure, with cerebral fungus and meningitis as inevitable consequences. But injection of air has done away with all these horrors. The neurologist has been forced to recognize its important place in correct intracranial localization and frequently demands its use by the neurosurgeon.

In two papers in 1923 and in 1925, Dr. Grant called this society's attention to these facts based on results obtained in the neurosurgical service in the University Hospital and from a collected series of 392 ventriculograms gathered from clinical material furnished by the Society of Neurologic Surgeons. Even at this early date, when neurosurgeons were still fumbling to perfect the technic of ventriculography, the percentage of otherwise unlocalizable tumors disclosed by this maneuver and later successfully removed by surgical methods was impressive.

In 1929 Dr. Gardner and Dr. Grant reviewed the results obtained by encephalography in evaluating the degree of damage sustained by the brain following trauma in cases of idiopathic epilepsy. These authors emphasized the fact that the lumbar insufflation of air is dangerous in the face of increased intracranial pressure and that hence this method should be avoided when a tumor, abscess or hemorrhage is suspected.

Trauma of the Brain.—In the early days of the society treatment of head injuries implied usually the management of fractures of the skull and trephining for epidural and subdural hemorrhages. The larger and more important problem —that of dealing with the effects of damage to the brain mass—was rarely discussed, much less comprehended. A number of instances were recorded in which the surgeon trephined for hemorrhage. Although one does not think of Dr. Deaver as a member of the neurosurgical guild, at a meeting of this society on Jan. 27, 1890, in closing his remarks on trephining for extradural hemorrhage he said that he wanted the society to understand that he was opposed to trephining in cases of focal epilepsy, tumors of the brain, etc. Then he proceeded to tell the members under what circumstances he thought trephining was justifiable. Trephining should be reserved for cases of fracture and hemorrhages.

The management of cerebral trauma, by which is implied cerebral concussion, contusion and laceration, has been revolutionized in the past ten or twelve years. Subtemporal decompression, once so popular, has been thrown into the discard, and dehydration has taken its place. Dr. Fay, at the January 1923 meeting of the society, first called attention to the administration of hypertonic salt solution for relief of intracranial pressure. Two years before he had introduced into the neurosurgical clinic of the University of Pennsylvania the use of magnesium sulphate as the dehydrating agent. Since that time he has contributed much to the knowledge of the application of dehydration not only in cases of trauma of the brain but also in cases of epilepsy. Magnesium sulphate is now used almost as a routine in cases of tumors of the brain with high pressure as well as in cases of trauma, and is often supplemented in emergencies by 50 per cent solution of dextrose. Both agents are indispensable.

Of particular interest to me, as to all neurosurgeons interested in the problems of cerebral trauma, are the histologic studies by Dr. Winkelman which were presented at the meeting of the American Neurological Association in 1933 (ARCH. NEUROL. & PSYCHIAT. **31**:956 [May] 1934). Dr. Winkelman found that in most of the cases in which the brain had been subjected to severe trauma there were definite histopathologic changes to account for the clinical findings. He had in mind principally the posttraumatic symptom complex which is usually characterized as a "traumatic neurosis." Even though the major injury might involve the cortex of the frontal or temporal lobe, the diffuse distribution of petechial hemorrhages not only throughout both cerebral hemispheres but in the cerebellar hemispheres, and in the pons and medulla was one of the important findings in Winkelman's study. He said that there is sufficient evidence in the brains of patients with severe trauma of the head to convince one that most of these patients have suffered organic changes to account for the symptoms so often observed as sequelae and too frequently regarded as of functional rather than of organic origin.

I shall refer briefly to what is now a well recognized surgical lesion, chronic subdural hematoma. All are familiar with Virchow's original contribution. At the meeting on Oct. 22, 1888, Dr. William Osler (*J. Nerv. & Ment. Dis.* **15**:608, 1888) presented a note on pachymeningitis haemorrhagica. He recognized two essential factors, the hemorrhage and the vascular membrane. He discussed the

source of bleeding and concluded that it is of dural origin. As to its frequency, Osler said that in eight years in the postmortem room of the Montreal General Hospital he had never seen a single case but in two or three months at the Philadelphia Hospital he had found 4 specimens.

In 1888, Dr. Dercum (*J. Nerv. & Ment. Dis.* **16**:174, 1888) called attention to 28 cases of hemorrhagic pachymeningitis in a series of 77 autopsies at the State Hospital at Norristown. In only 4 were there large hematomas.

At the meeting in December 1913 Dr. Spiller described a case of extensive bilateral subdural hemorrhage over both cerebral hemispheres without motor paralysis or irritation. The history was typical of what is now called chronic subdural hematoma: a blow on the head without loss of consciousness a month before, with continued headache and vomiting, followed later by drowsiness and finally unconsciousness. Because of the absence of signs of fracture of the skull, the unconscious state of the patient and the history of alcoholism, surgical intervention was not considered, but at necropsy an extensive bilateral hemorrhage was found over both frontal, motor and parieto-occipital regions. In the same year Dr. J. H. Lloyd exhibited a specimen with a large subdural hemorrhage.

Whether or not it is because the etiology and the clinical syndrome now are so well comprehended, the incidence of the lesion has increased to no small degree in the past decade. From the neurosurgical clinic in the past four years several contributions on this subject have come from members of the staff, Dr. Grant in 1930 and Dr. Rowe and Dr. Frazier in 1934. The latter authors reviewed experiences with 6 cases that had been observed in the past two years and called attention to certain salient features. There is usually a preexisting trauma, trivial though it may be, followed by persistent headaches, occasional vomiting, sometimes papilledema and later somnolence. The lesion is bilateral in 50 per cent of the cases; the clot is usually in front of the rolandic fissure; there may be no localizing phenomena, or should there be signs of pressure the symptoms may be contralateral or ipsilateral. Even though the lesion is bilateral the symptoms are often unilateral. Even tumor or abscess of the brain has been considered in some cases to be the responsible factor. Time will not permit more than passing mention of contributions on that interesting topic spontaneous subarachnoid hemorrhage, such as those of Dr. Clemens (November 1929), Dr. Harlow (September 1932) and Dr. Langdon and Dr. Cooper (November 1934).

Epilepsy.—Even in 1886 operations were recommended for the treatment of epilepsy. In the case reported in that year by Dr. Mills, in which the convulsions followed a gunshot wound, an operation was performed. Incidentally, it was noted in the history, as it seems to be noted in many histories of that time, that the patient was given to the use of alcohol and had been since he was 18 years of age. In this case the operation was performed on the theory that the epileptic seizures were due to irritation of the dura, which in turn was supplied by the branches of the fifth nerve. Quoting from Duret in an article which appeared in the first volume of *Brain* in 1878, it was said that specimens have shown that powerful stimulation of the dura mater would cause movements in both sides of the face, in the neck and in the four extremities. At the operation spicules of bone were removed from the dura mater. As in the case reported to the society by Dr. Reed Harrow (December 1930), the accepted method of dealing with traumatic epilepsy, following the suggestion of Foerster and Penfield, involves the liberal excision of the cortical scar.

Much has been heard in recent years of vascular lesions of the cerebral cortex, many of which have been grouped under the term aneurysm. These are not aneurysms in the sense that they are saccular dilatations of the vessels but more in the nature of varicosities, usually involving the veins. This lesion is frequently associated with convulsions. In the proceedings of the society for April 23, 1909, Dr. Alfred Gordon reported a case in which the epilepsy was alleged to be due to a varicose state of the cerebral veins. In the case under consideration the veins were ligated, and this in turn was followed by hemiparesis and aphasia. This

was the first occasion on which the relationship of cortical varicosities to epilepsy was brought to the society's attention or had been mentioned elsewhere.

The Hypophysis.—The hypophysis was not ushered into the discussions of the Philadelphia Neurological Society until it had reached the half-way mark in 1910. Prior to that time there were several references to the sella turcica, which presumably had to do with the hypophysis; the first was made, I think, by Dr. Morris L. Lewis in April 1885, who described "Necrosis of the Sella Turcica with Brain Softening." The original does not seem to be available, and just what the author had in mind when he spoke of necrosis of the sella turcica cannot even be surmised. Some years later (December 1897) tumors of the hypophysis were for the first time introduced into the programs in a paper by Dr. W. E. Hughes.

Many will remember the startling report by Dr. de Schweinitz of the apparent cure of complete blindness in nineteen days "by large doses of thyroid extract." The patient had a hypophyseal tumor. At the time the report made a great impression on me, but the cure was, as de Schweinitz said, only apparent. The visual defect returned, and it has generally been assumed that the temporary restoration of vision was due not to the feeding of thyroid but to spontaneous decompression of the tumor into the sphenoid sinus. The society was becoming hypophysis-minded, for on the same evening Dr. S. D. Risley spoke for the first time of bitemporal hemianopia with acromegaly and other symptoms as probably due to hypophyseal lesions, and two years later, in March 1912, two contributions appeared, one by Dr. J. C. Knipe and the other by Dr. J. H. W. Rhein; one described interesting ocular symptoms with hypophyseal dysfunction, and one, bitemporal hemianopia.

The hypophysis has been the target at which innumerable research problems have been directed for the past twenty-three years, and among the first of them was that presented by Dr. A. R. Allen and Dr. J. E. Sweet in a paper entitled "Effect of Removal of the Hypophysis on a Dog" (November 1912). This research aroused much discussion at the time for the conclusions at which they arrived were at variance with the conclusions of research in other quarters. The point at issue was whether the hypophysis was essential to the maintenance of life. Dr. Sweet and Dr. Allen, with a number of others, maintained that it was not. In a summary the authors said: "We are presenting this paper at the present time for two reasons: First, we believe that the question of the essential or nonessential nature of the hypophysis is an important surgical matter, and from the results of our work we believe that the entire gland can be removed without danger to life. In the second place, from our work we believe that there is but one surgical indication for operating, namely, intracranial pressure. If such experimental experience is of any value it is that the intracranial method of approach is to be preferred to any other method, and that the method of operation in human cases, which has been elaborated by Frazier, is undoubtedly the most correct from the point of view of anatomy and of surgical technic."

In 1912 the first operation for relief from symptoms due to hypophyseal tumors was practiced in the neurosurgical clinic, and in January 1913 I was privileged to present to the society the first paper on this subject of surgical interest. The paper is interesting only as illustrating an early period in the elaboration of the technic. Since that time the method of approach has been revised many times, until today the operation, as now practiced, seems to have fulfilled every requirement as to safety, as to rendering the hypophysis accessible and as to the ultimate cosmetic effect.

The tumor described by Dr. Grant and Dr. Lloyd at the meeting in February 1924 was of interest chiefly because of its extraordinary size. The tumor, an adenoma, measured 5 by 9.5 cm. and extended far beyond the confines of the sella turcica, into the interpeduncular space, the pons and cerebellum, the temporal lobe and bones at the base of the skull. From this description, one would suspect that the tumor might have been an adenocarcinoma rather than a benign adenoma.

In a paper on the surgical procedures on the pituitary gland presented in January 1923 Dr. C. H. Frazier reported a series of cases representing many phases of hypophyseal dysfunction. The paper was of interest chiefly to the neurosurgeon,

as marking that period in the evolution of hypophyseal surgery when the transsphenoidal approach, as described by Hirsch, was used exclusively.

At the time of their presentation in April 1922, the observations of Dr. Grant and Dr. Fay attracted wide attention, though they were of interest chiefly to the ophthalmologist. In a well illustrated article the authors described certain bizarre fields which were attributed to the effects of pressure by adjacent vessels.

From the neuropathologic laboratory, under the direction of Dr. Bernard J. Alpers, there have issued a number of worth while contributions. One of these included the exhibition to the society of a patient who was the first, I believe, to be presented with a syndrome which at that time, April 1933, was attributed to a basophilic adenoma—a syndrome first described by Cushing. Since then much skepticism has arisen as to whether this minute lesion plays any part in the syndrome. Its counterpart has been attributed by others to lesions of the adrenal glands. To me the most important of Dr. Alpers' contributions have to do not with the hypophysis itself but with lesions of the hypophyseal stalk and Rathke's cleft. His report to the society in March 1931 of 14 cases of adamantinoma (stalk tumors) gathered from the 244 cases of sellar and parasellar lesions in the neurosurgical files was notable in many respects. The last product of his laboratory is one of no little significance to those interested particularly in the anatomy and pathology of parahypophyseal lesions. For reasons supported by substantial evidence he has defined the conditions to which the term tumor of Rathke's pouch should be restricted. At the same time he proposed the adoption of a new nomenclature in which the term "craniopharyngioma" (a misnomer) gives way to "hypophyseal stalk tumor" and "tumors of Rathke's pouch" to "tumors of Rathke's cleft."

Abscess of the Brain.—Although abscess of the brain is an important and not infrequent intracranial lesion, it is curious how rarely it has been commented on before this society. Possibly this is due to the fact that abscess of the brain so commonly accompanies disease of the sinuses or mastoid that its treatment has been considered a part of rhinology and otology. In January 1916 Dr. Cadwalader and Dr. Rodman described a case of cerebral abscess with recovery following operation. In 1929 Dr. Grant reported a case of cerebellar abscess with recovery, and in 1931 he surveyed his material and that from the neurosurgical service at the University Hospital. In the latter communication, 40 cases of abscess were reported. In 20, immediate drainage was instituted, with 2 recoveries. In the other 20 cases, time was allowed for encapsulation, and 14 patients recovered. The lowered mortality was due apparently not to more accurate localization but especially to sufficient delay in the institution of drainage to permit encapsulation of the abscess. Very few cases of abscess of the brain present surgical emergencies. Careful observation permits the surgeon to obtain a much more satisfactory opinion as to the position of the abscess and, of even greater importance, allows the brain sufficient time to wall off, localize and encapsulate the infection.

Tumors of the Brain.—As one reviews the contributions of the older members of the Philadelphia Neurological Society on surgical procedures on the brain, there are certain facts which become rather vividly impressed on one's mind. These are: 1. The clinical facts of today, the fundamentals and raw materials on which diagnoses are based, were the objects of wonder to the older members and led to investigations and reports which serve frequently as guides today. What seems more natural today than to accept homonymous hemianopia as a localizing sign of the first importance? Yet forty-five years ago it was still a matter of debate among older members, debate which led eventually to clarification and to the passing down of a heritage of clinical facts now accepted because of the pioneer investigation of the older members. Some of these facts will be pointed out as I proceed. 2. Neurosurgery itself is a very young subject, so young in fact that the majority of the real contributions have come since 1916, and most of them much later. It is interesting to observe further that as the neurosurgeon has become more and more interested in the physiology of the brain and in the clinical aspect of his own subject, under these conditions he has initiated many sound

clinical ideas useful both to himself and to the neurologist. In the development of this the youngest of the family circle, the members of the Philadelphia Neurological Society have played significant and sometimes important rôles.

Some of these facts are illustrated by cursory chronological review of the contributions of members of the society to neurosurgical subjects. Dr. Mills in 1887 (*J. Nerv. & Ment. Dis.* **14**:707, 1887) reported 2 cases of tumor of the brain in which there was complete facial paralysis in the upper part of the left side of the face and in the left arm and leg. The second case was that of a tumor of the thalamus with paralysis of the upper part of the face in association with hemiplegia. Dr. Mills, with his philosophic bent, emphasized the association of this type of weakness in some cases of hemiplegia.

A very early record of tumor of the olfactory groove is found in a case reported by Dr. Morrison in 1893 (*J. Nerv. & Ment. Dis.*, 1893, p. 76). According to the case record the growth was a large intracranial tumor compressing the left frontal lobe; it occupied almost the entire anterior fossa, eroded the left cribriform plate and communicated with the nose. Of particular interest is the fact that the pathologic report was made by Dr. Burr, who classified the tumor as a sarcoma, as fibroblastomas of the arachnoid were classified in those days.

In 1893 Dr. Burr (*J. Nerv. & Ment. Dis.*, 1893, p. 90) raised a problem which is unsolved today, namely, the differentiation of tumors of the frontal lobe from cerebellar tumors. The clinical localization was cerebellar; necropsy disclosed a tumor in the right prefrontal region; Dr. Dercum, in the discussion, pointed out the difficulty of distinguishing between tumors of the frontal lobe and cerebellar tumors and mentioned a case in which exploration by the frontal route subsequently revealed a cerebellar tumor. Despite all that has been written since then concerning the frontocerebellar pathways, the clinical differentiation of some tumors in these widely separated areas is as difficult today as it was in 1893.

In a paper on glia and gliomatosis, Dr. Flexner (*J. Nerv. & Ment. Dis.*, 1898, p. 306) described ependymal gliomas and ependymal cells about four years before Mallory's classic description of these tumors. In 1898 Dr. Lloyd, in commenting on a tumor of the cerebral dura by Arnold, remarked: "Looking at the specimen, it is easy to regret that the patient was not operated on." In the same year Dr. Diller presented a case of alcoholic serous meningitis simulating tumor of the brain. No operation was performed. In this year, also, the customs of the times were reflected in a report by Dr. Dercum entitled "A Cerebellar Tumor, One of the first Manifestations of which was Ataxia While Riding a Bicycle." There was nothing unusual about the tumor except that it was thought to be tuberculous.

In what was apparently a "brain tumor" meeting in 1901, contributions were made by Drs. Wharton Sinkler, Dercum, Mills and John K. Mitchell. Dr. Sinkler reported 2 cases of dementia paralytica simulating tumor of the brain, both with jacksonian convulsions. This practical subject is of interest even today, for many a case of jacksonian fits is suspected of being one of tumor of the brain and later found to be one of dementia paralytica. In Dr. Dercum's case the growth was probably a large glioblastoma multiforme of the occipital lobe, which seemed to merit recording because it caused hemiparesis as well as hemianopia. On this occasion Dr. Mills made some general remarks on the localization of tumors of the brain, especially with reference to the parietal and prefrontal regions, based on 5 cases in which the sites of the tumors were located for the purpose of operation. Today it seems utterly unnecessary to report instances of this sort, but it must be recalled that the location of the motor cortex was by no means as well defined in 1901 as it is today, and the sensory functions of the parietal lobe with its stereognostic center were clarified in part only by patient clinical research by Dr. Mills and others. Much of the security of today in matters of clinical localization is due to the investigation of the seemingly obvious of yesterday by our distinguished predecessors in this society.

In 1909 Dr. Weisenburg (*J. Nerv. & Ment. Dis.*, 1909, p. 301; 1910, p. 49) defined the syndrome of tumors of the third ventricle, a contribution which has

served as the starting point for subsequent investigations of tumors in this region. At the time of this report no clinical criteria for the recognition of these tumors were known. Dr. Weisenburg defined their syndrome and made possible accurate localization of tumors of the third ventricle. In 1911 he (*J. Nerv. & Ment. Dis.* **38**:548, 1911) reported a case of tumor of the right occipital lobe with unformed visual hallucinations in the left hemianopic field. These hallucinations comprised jumbled colors, darkened glass, a lot of bricks, etc. One of the interesting features of the report was the discussion by Dr. Spiller, who remarked that the case was of great interest because for a number of years he had been uncertain whether visual hallucinations were always on the side opposite the occipital tumor. Here is another instance of the preparation of facts for future generations to use.

In 1910 Dr. Weisenburg (*J. Nerv. & Ment. Dis.*, 1910, p. 452) reported his famous case entitled "An Unusual Case of Tumor in the Cerebello-Pontine Angle Which for Many Years Gave Symptoms of Tic Douloureux and the Symptoms of Irritation of the Ninth and Twelfth Nerves." Here was defined for the first time the syndrome of neuralgia of the glossopharyngeal nerve, which has been confirmed subsequently by many other investigators, all of whom give Dr. Weisenburg priority in the definition of the syndrome.

That the accepted facts of today are the mysteries of yesterday is shown in a case of a tumor of the parietal region reported by Dr. Lloyd in 1912 (*J. Nerv. & Ment. Dis.*, p. 617), in which no motor symptoms were present throughout the course. He remarked that the case was an interesting confirmation of the theory that the motor centers are entirely anterior to the rolandic fissure. Little do students realize the effort and time consumed in establishing what are to them established facts. Who doubts Lloyd's statement now? Yet who bothers to think about Elliot Smith's investigations in comparative anatomy, Sherrington and Ferrier's physiologic studies, or Holmes' clinical investigations; all of which a number of years ago established what now are the A B C's of neurology.

In 1912 Dr. Lloyd and Dr. Hammond (*Am. J. Med. Sc.* **143**:241, 1912) reported a case of tumor of the brain successfully located by means of the roentgen rays. This was a case in which a calcified tumor was clearly outlined. This seemed to be a remarkable finding, for the authors remarked that so far as they knew no case of tumor of the brain in which the shadow was so clearly shown had yet been reported. Operation revealed a cyst which was emptied of clear fluid. The authors reported that deep within this cyst cavity a hard bony mass was felt. This was also palpated by Dr. Charles H. Frazier, who witnessed the operation.

If one analyzes the contributions up to 1912 or thereabouts, one finds that the emphasis has been largely on diagnosis and localization, the neurologist's contribution to neurosurgery. By careful study of cerebral functions he has made possible the logical interpretation of signs so that exposure of the brain for the disclosure of a tumor might be removed from the realm of the haphazard. Surgical measures on the brain as such did not exist up to this time. From 1921 on, the neurosurgical contributions have assumed a totally different character, for the neurosurgeon has been trained and the exploratory craniotomy has come to be accepted as readily as the exploratory laparotomy. The recent contributions seem to be of two sorts: (1) those indicating the possibilities of neurosurgery, shown by the recording of successfully removed tumors, successfully treated pain, etc.; (2) those defining more clearly the clinical syndromes of tumors of the brain, thanks to the opportunities for the study of the large series of cases in the neurosurgical clinics.

Thus in 1921 Dr. Frazier reported a series of tumors of the brain and spinal cord successfully removed, 1 a tumor of the brain of diminutive size (2 by 3 cm.) and another a gigantic tumor measuring 10 by 13.6 cm. In 1922, Dr. Grant recorded a gliomatous cyst which was outlined by the injection of air and localized readily by the roentgen rays. The importance of hemianopia as a localizing sign was emphasized in this year by Dr. Hammond and Dr. Lloyd and by Dr. Mills in the discussion of their paper.

In 1923 two contributions were made by Dr. Spiller on a "Meningioma, Both Intradural and Extradural, Removed from the Spinal Cord with Complete Recovery by Dr. C. H. Frazier" and "Enchondroma of the Left Motor Area Removed with Recovery."

In 1925 Dr. Patten reported a case of a meningioma of the right frontal region in which there had been a history of headache for from twenty to thirty years. Two years later, in 1927, Dr. Weisenburg raised the question whether the higher psychic functions are localized in the frontal lobes. He doubted whether they were. The paper called forth a retort from Dr. Mills, who defended the localization of higher functions in this area, for Dr. Mills was a warm proponent of cerebral localization.

There then follow reports of successfully removed tumors by Dr. Grant (1927, 1928), by Dr. Kwan (1929), his tumor being a tuberculoma removed eleven years previously, and by others. In 1928 the presidential address by Dr. Burns was concerned with a careful analysis of the diagnostic measures utilized in the localization of tumors of the brain. Dr. Gardner, in 1928, reported the detection of tumors of the angle by means of the Tobey-Queckenstedt test, demonstrating a block on the side of the tumor. But of the many contributions on tumors of the brain especial mention should be made of that member of the second generation of neurosurgeons Dr. W. J. Gardner (Gardner, W. J., and Frazier, C. H.: Bilateral Acoustic Neurofibroma, ARCH. NEUROL. & PSYCHIAT. **23**:266 [Feb.] 1930). His field study of a family of five generations with bilateral deafness in 28 members was important as a contribution both to the science of heredity and to the knowledge of bilateral tumors of the acoustic nerve.

In recent years there have been presented before the society a number of contributions concerned with the clarification of the syndromes of tumor of the brain in certain definite regions of the brain. All have been instructive; some have been valuable. These studies include Dr. Kubitschek's analysis of the symptomatology of tumors of the frontal lobe, in which it was asserted that these lobes are not concerned with the higher psychic functions. This drew fire from Dr. Mills, who insisted on the localization of the higher psychic functions in the frontal areas. There followed in 1929 the analysis of 40 cases of tumor of the occipital lobe by Dr. Frazier and Dr. Waggoner, and of 52 cases of tumor of the temporal lobe by Dr. Rowe. Both these studies crystallized knowledge of these groups of tumors. In 1931 Dr. Duane reported on the ocular manifestations of tumors of the occipital lobe, indicating the difference in the field cuts of tumors of the temporal and occipital lobe. In 1933 Dr. Alpers and Dr. Groff reported before this society the syndrome of fibroblastomas of the sphenoid ridge, defining clearly the clinical manifestations of encapsulated tumors in this area.

The subject of "pseudotumors" has been one of absorbing interest. This lesion is sometimes styled arachnoiditis, but the term "pseudotumor," as proposed originally by Nonne, is much more descriptive and should be given preference. This subject was first mentioned in the proceedings of the society in January 1925, when I showed the effects of a cerebral decompression on a patient of Dr. de Schweinitz'. The high grade papilledema disappeared with amazing rapidity; that patient since has graduated from college, has married and is now free from symptoms. Later, in April 1930, I presented to the society a series of 25 cases (Cerebral Pseudotumors, ARCH. NEUROL. & PSYCHIAT. **24**:1117 [Dec.] 1930) and called attention to the extraordinary way in which these circumscribed collections of fluid could mimic solid tumors. In every case but one the operation was followed by permanent relief. More recently, at a Mütter lecture, I described suprasellar pseudotumors which give rise to symptoms that might be suspected of being of hypophyseal origin.

Comment: Though lengthy, how imperfect this sketch has been. Surely in these fifty years the members of this society have seen neurosurgery, once in its infancy, become a well recognized, rapidly growing, rapidly expanding calling. At the beginning the neurosurgical clinic in Philadelphia was one of but two in the country. There are now three well established clinics in Philadelphia alone and

others in all the larger medical centers of the country and new ones cropping up every year with amazing frequency. In the old days the members of the society were absorbed with the tumor of the brain as it appeared at the autopsy table; today it is the tumor of the brain exposed in the living subject. The neurosurgeon has outgrown the stage of his growth at which matters of technic absorbed most of his interest. He has higher ambitions now and is utilizing every opportunity at his command to contribute to physiology, to pathology and to symptomatology, as well as to treatment. He is playing his part as a side-partner of the physiopathologist on the one hand and the neurologist on the other. He needs the cooperation of both, and with the three working in perfect harmony one may anticipate for the future a wholesome and productive family life.

PSYCHIATRY IN THE PAST FIFTY YEARS. DR. CHARLES W. BURR.

I shall review briefly the state of knowledge and opinion half a century ago, as an old man thinks his young self saw it, and relate what discoveries in causation, what improvements in treatment and what changes in opinions and in point of view have taken place since. This would be an easy task provided man were, in truth, a thinking animal. Unfortunately, man is a feeling animal, the slave of his heredity, the victim of his environment and largely controlled by bias and not by reason. A man of different origin, one whose life had been subject to other conditions, would hold other views than mine.

A half century ago psychiatry was still merely descriptive, and the majority of physicians were still under the influence of a spiritualistic philosophy; a few were grossly materialistic. People in general had more than a lingering belief that there was something disgraceful in "insanity" and that, may be, the old religious belief that it was sent in punishment for sin was not altogether erroneous. Psychologists had already learned from physiologists that there are cerebral centers and had begun to tie up discoveries in cerebral localization (motion, sensation, speech and the special senses) with mental function. One kind of dementia was proved to be associated with word deafness, and soon ordinary blindness was separated from mind blindness, but most psychiatrists paid little attention to the work being done in psychologic and still less to that being done in physiologic laboratories. They used up their energy in assembling groups of symptoms and calling them diseases. The greatest advance has been in the change of attitude and the method of approach. Little attention was paid to studying mental processes in normal persons, and the psychotic persons were regarded almost as a race apart; it was not dreamed, save by a few students, that the study of the normal would throw light on the abnormal. Dr. Freud, whose philosophy I do not find myself in sympathy with, deserves credit for stimulating the clinical study of normal psychology. His own conclusions have not stood the test of one generation, but he did much to make the study popular and deserves credit for this, no matter how baseless his assumptions and how erroneous his resulting opinions.

At the time of the founding of the Philadelphia Neurological Society, all physicans in private practice who were neurologists were also psychiatrists and had been in general practice, and the best doctors in asylums, although they did not practice neurology, were interested in it as a scientific matter. It is worth noting that the word "psychiatrist" had not yet come into use, and "asylum" is now obsolete. Dr. Isaac N. Kerlin, superintendent of the Elwyn Training School, was elected acting chairman at the meeting for organization, held on Dec. 15, 1883, and at the January 1884 meeting he and Dr. Charles K. Mills were elected vice-presidents. Dr. John Chapin was elected to membership in November 1884, soon after coming to this city to become head of the department of mental diseases of the Pennsylvania Hospital. Again, as showing the interest in mental disease, the first paper read at the first stated meeting on Feb. 25, 1884, was by Dr. Mills, its title being, "The McGinnis Case." This paper seems to have discussed insanity and crime. On Feb. 23, 1885, Dr. Mills presented a paper entitled "The Brain of James Burke, a Delusional Monomaniac, Who Had Killed Some Person and Who Lost His Life in the Recent Almshouse Fire; and Also the Brain of an Uxoricide

Recently Executed." There are two interesting words in this sentence; one shows changes in scientific nomenclature; the "monomaniac" would now be called "paranoiac." The word "almshouse" illustrates the modern notion, that if a thing's name is changed the thing is changed. The word "almshouse" has been abolished; the thing, pauper, has been retained.

Dr. Mills was frequently called as an expert to give an opinion in cases of criminals alleged to be insane, and he read several papers on this subject before the society. Public opinion concerning mental experts, never very favorable, has grown more and more antagonistic, until today it is contemptuous. There are several reasons for this. One, a minor reason, is that the law retains many conceptions that increasing knowledge has proved to be false. But the most important reason is that a few dishonest, but intellectually acute, physicians are willing to give, for a price, any opinion desired and to support it with plausible arguments. Fortunately, courts, judges and juries are beginning to learn something about the real relation of crime to insanity and are acting accordingly. The Municipal Court in Philadelphia has done pioneer work in this matter, so that young offenders are examined as a routine practice by physicians who are officers of the court and whose opinions do not and cannot depend in any degree on a fee.

In March 1885 Dr. A. W. Wilmarth read a paper on "Malformations of the Idiot Brain" and presented specimens, and in October 1885 Dr. Henry M. Wetherill read one entitled "Notes on the Action and Use of Hyoscine in Insanity." In February 1887 Dr. Isaac N. Kerlin read a paper on "Moral Imbecility," a subject which today is again attracting much attention, and Dr. Wilmarth read one on "Morphology and Pathology of Idiocy." It would be tiresome and of little value for me to give all the titles of papers read during the past fifty years. Suffice it to say that Philadelphia psychiatrists have continued through the history of the society to show a real and practical interest in it. There was at one time, but only for a short period, a little bad feeling. When in 1909, after Dr. Buckley had talked over the matter with me, I decided to form a psychiatric society, my friend Dr. Mills opposed the project and, for him, became quite peevish. I grew obstinate. The psychiatric society was founded. Both Dr. Mills and I soon stopped secreting too much epinephrine, and both societies have flourished.

What advances in therapy have been made in the last half century? I presume that every one would say that the most striking step forward has been the introduction of arsenicals administered intravenously. At first, arsphenamine was heralded as a cure for syphilis. The claim has not been proved. Certainly many syphilitic persons have been relieved from symptoms; the signs of disease, or some of them, revealed by examination have sometimes disappeared, and the patient has continued without signs or symptoms for a shorter or longer time and occasionally has died of some other disease. Sometimes, on the other hand, a patient undoubtedly syphilitic not only has been refractory to arsenic but has been definitely injured by it. The history of dementia paralytica during my professional life has been interesting. When I began to practice the old name "general paralysis of the insane" was still in common use. Often it was abbreviated to "paretic dementia." Many physicians realized the close causative relation of syphilis, but all textbooks gave a long list of causes—excessive venery, business and family stress and strain, worry, drinking and the like. As time passed, more and more writers emphasized the importance of syphilis and the unimportance of other causes, until finally the dogma "no syphilis, no dementia paralytica" came to be universally accepted among medical men. This opinion still rules. Juvenile dementia paralytica was unrecognized as such and was often called "syphilitic imbecility."

The conception of the clinical picture of dementia paralytica has changed mightily. Fifty years ago the typical picture was dementia occurring during maturity and associated with grandiose delusions. On the physical side one expected to find no signs of visceral syphilis, but a slurring speech, abnormal pupillary and patellar reflexes, epileptiform convulsions, transient aphasia and cerebral palsy and, not infrequently, transitory and apparently causeless fever. Periods of freedom from mental symptoms were not infrequent. Death was inevita-

ble and the average duration of life three years. As time passed it was found that some patients showed no delusions but presented simple dementia as the only mental symptom, and at about the same time in other patients expansive and grandiose delusions were being proved to be replaced by depressive delusions. All the time evidence was piling up that syphilis was the cause. The introduction of the Wassermann test of the blood and the spinal fluid proved the truth of the saying "no syphilis, no dementia paralytica," and at the same time broadened the conception of its clinical picture, until today the diagnosis is based by many physicians solely on the laboratory findings (four plus reaction of blood or spinal fluid, with positive colloidal gold curve), no matter what the mental picture may be. But though syphilis must be present, there is also another causative factor necessary, the protoplasmic nature of the patient, an inborn, inherited thing. The protoplasm must have the predisposition, or dementia paralytica will not result. Only thus can one explain the fact that many syphilitic persons escape having dementia paralytica, and this whether there has been much or little treatment, good or bad, by old methods or new, and no matter how long after the initial sore the patient lives. The new chemistry will solve this problem. In what is called, of course unjustly, the dark ages of fifty years ago, all physicians separated cerebrospinal syphilis from dementia paralytica, which was regarded as a sequel of syphilis and not syphilis itself. Textbooks gave elaborate tables of differential diagnosis. One great point was that in dementia paralytica mental symptoms always preceded physical symptoms, while in nervous syphilis the reverse held. If the patient recovered, the condition was said to be syphilis, and many patients did recover under therapy with potassium iodide, given in rapidly increasing doses, sometimes reaching more than 100 grains (6.5 Gm.) daily. Today it is claimed by some authorities, and by many who are not authorities, that dementia paralytica is a curable disease, if not by the administration of arsphenamine then by the administration of neoarsphenamine or some more recently invented arsenical compound. Curiously enough, however, notwithstanding the alleged brilliant results, the use of bismuth and other metals is coming into popularity.

Then came treatment by the artificial production of fever by inoculation with the organisms of malaria or typhoid or by mechanical means. This also sometimes gives excellent results, but as a rule they are temporary.

It is undoubtedly true that all these newer treatments occasionally cause, or at least their use is followed by, wonderful results. But it is also true that as a rule dementia paralytica ends in deaths and should not be called a curable disease.

A curious thing followed the introduction of arsphenamine and its allied chemical successors, namely, a real, or apparent, increase in the frequency of dementia paralytica. One explanation is that arsphenamine given in the early stages results in apparent, not real cure, and hence more syphilitic persons live long enough to have dementia paralytica. I believe that there has been a great increase in the frequency of this condition, but it is unproved that the use of arsenicals has much to do with it. There has been an increase of syphilis itself, and hence of dementia paralytica, because of the letting down of the moral bars, the increase of amateur prostitution and, until recently, an increasing flow of immigrants, already infected at home and acting as foci of infection in this country. The change in the manner of living among Negroes has greatly increased the disease among them.

The use of continuous warm baths in cases of mental disease, which is really a rediscovery of something known centuries ago, is one of the greatest aids in quieting excitement which the last fifty years has given. It has none of the evils of sedation induced by drugs and often acts almost miraculously.

The experiments in shortening attacks by continuous sedation induced by drugs, almost to the production of coma, seemed at first to give great promise, but the method has not stood the test of time.

The movements for improving the condition of the insane in institutions have since the time of Tuke been largely started and supported by laymen. Our fellow member, Dr. Charles Frazier, not a layman but not a psychiatrist, has of recent years given much time and thought to this, and our society has devoted several meetings to the Committee on Mental Hygiene.

No school of psychology has had as wide and sympathetic an audience as that headed by Freud, especially among that class of people, so large in America, who like to read and have a real craving to be scientific but who have not been taught how to think. The sober-minded and reserved English, the logically minded French, and the older Germans, before war and revolution came, were influenced in much less degree by the writings of Freud than were the Americans. Kohler and his *Gestalt* psychology made a greater appeal to persons thoroughly trained in scholastic and laboratory psychology. But Freud was so simple, so easy to understand, that no training was needed. The freudian is born. Freud made three assumptions: the subconscious, dream symbolism and libido. What Freud called the unconscious is largely bias; it is the personal attitude that a man assumes emotionally and also, in turn, the reaction that attitude has on him in his approach to every question and feeling in life. It has nothing to do with the intellectual and reasoning functions of the mind. There is quite a little evidence that unconscious thinking does occur, but this is very different from the subconscious of Freud. An excellent example of such unconscious thinking is shown in Livingston Lowes' "Road to Zanadu." Lowes' object was to search out the original sources of Coleridge's "Ancient Mariner." He was not writing a book on psychology and had no interest in the technical side of the matter but was interested in where Coleridge found his descriptions of sunsets and sunrises at the poles and the equator, the effect of light shining through breaking waves, old seaman's lore and the hundred and one remarkable things described in that poem. Coleridge had a prodigious memory and a note book. Lowes studied the latter, read the books therein referred to, many of them by old travelers who wrote in the time when great exploration was going on and who told strange tales of men met with and things seen, and found the data. Coleridge did not think out "The Ancient Mariner" during all those years he was reading. A possible explanation, and one that appeals to me at least, is that, given the type of man that Coleridge was, including the influence of tincture of opium as affecting the final nature of the poem, his mind unconsciously drew from memory these many isolated facts and assembled them all unknown to himself, and then conscious work began and the poem resulted. Do not ask me the mechanics of this process, because I do not know, but this kind of subconscious appeals to me much more than the freudian.

Freud's dream symbolism and libido are tied up together. During waking hours, what Freud called the censor keeps a man in slavery and prevents him by taboos, which really do not need a censor either to prove or to justify their existence, from acting his own real part. In sleep the censor disappears and sinks into one unconscious to give the other unconscious freedom. The dream reveals the man. Dreams are not what they seem. They are, according to Freud, symbolic, and long thin things mean an organ and a desire to use it. Now long thin things, umbrellas, canes and the like, are common in dreams. Frankly, such explanations of the dream state make one think of the intellectual and moral level of the brat-minded. The dream interpretations of early man and of the uncivilized races of today were and are much cleaner and more reasonable. That the loss of sex inhibition is almost universal in mental disease and sex aberration common is well known, but one does not need dreams and the censor to explain it. Suppression may and does work evil, but it needs no mysterious explanation. The oedipus complex is historically incorrect and the castration complex without the slightest proof of ever occurring, save in the minds of psychoanalysists and thence transplanted into the thought of patients susceptible to suggestion. I speak strongly on this matter because I have seen not a few people incurably injured by psychoanalytic treatment by freudian disciples. In Freud's own defense it ought to be stated emphatically that he did not teach the use of psychoanalysis in psychoses.

May I wander a little from my subject, the past, and speak briefly of the future and the hope it holds? I do not think men of my own professional class, physicians of the nerves and mind, will advance knowledge as to causes. They will recognize and record the changes in the clinical pictures as civilization changes, discover new

symptoms and signs and test out therapeutic measures. They will seize discoveries which other men, trained on different lines, will make. Science will continue to be a tool for them, but it will be created by minds of other types. One can look for no help from metaphysicians and their bastard brothers the sophists, who today are just as numerous as they were in old Greece, make just as much noise and get just as much popular acclaim. I do not wish to be like Professor Monroe, of Edinburgh, who more than one hundred years ago said, "Anatomy is a completed science," when really it was just beginning to become a science, but I do not think any fundamental discoveries throwing light on mental processes are going to come from further microscopic study of the brain. Remember, I say fundamental; minor discoveries doubtless will be made.

After all, is not the cause of acquired mental disease seated in other organs and the brain put out of order by things acting on it rather than by things arising in it? Of course, I am excluding undeveloped or grossly traumatized brains.

The main hope lies in biochemistry. When there is known, as there will be, a great deal more about the chemical functions of the ductless glands especially, and of all organs in general, then much will be learned about what one may call the secondary processes of thought and feeling and their disorders. But even then, even to the end of time, unless a god comes to earth and reveals it, the fundamentals of human thought, its real mechanics, how the brain thinks, will remain unknown, even as it was to our superiors, the great men of the day of those two contrasting and complementary geniuses Plato and Aristotle, unless, indeed, the mathematicians win their way and prove that men are only mathematical formulas and have no real existence. That would mean going back to the guess of Protagoras, and the circle would have gone full round.

Book Reviews

Les ramollissements protuberantiels. By J. O. Trelles. Price, 50 francs. Pp. 308, with 100 illustrations. Paris: Gaston Doin & Cie, 1935.

This volume is concerned only with the the syndromes of softening in the pons. A short section is devoted to the history of the subject and to the anatomy and blood supply of this part of the brain. The syndromes are divided into four types, the basis for the classification being the vascularization of the pons as determined by Foix and Hillemand, viz., paramedian, short circumferential and long circumferential vessels. The syndromes are: (1) those consequent on softenings in the paramedian area, (2) those of the short circumferential vessels, (3) mixed syndromes and (4) those of the long circumferential vessels. The etiologic factors are chiefly arteriosclerosis and syphilis.

The chapter devoted to pontile hemiplegia emphasizes that this type of hemiplegia has characteristics which are peculiar to it alone. Among them are the complete absence of aphasia in right-handed persons with a right hemiplegia, absence of loss of consciousness at the onset of the hemiplegia, absence of evidences of deterioration and persistent spasticity of the limbs. It is difficult to see, however, how any of these features differs radically from those which characterize an ordinary capsular hemiplegia, for in this condition too there is no aphasia, though there is usually definite evidence of intellectual reduction. Trelles points out that the pontile hemiplegias are due to occlusion of the paramedian branch of the basilar artery, the mesial fillet escaping completely. On the other hand, pontile paraplegias are very uncommon and indicate that in the pons, as in the internal capsule, there is a somatotropic arrangement of the pyramidal fibers, those to the lower limbs lying in the ventral portion and those to the upper limbs in the dorsal portion. The clinical syndromes resulting from the occlusion of the circumferential vessels are not as definite as in the hemiplegias and paraplegias.

The classic syndromes of the tegmentum of the pons are mentioned briefly. Lengthy consideration is given to the problem of palatal myoclonus. The monograph is a useful compendium of published cases of pontile softening and contains a complete bibliography. It is profusely illustrated, though many of the illustrations are repetitive. Unfortunately, there is not too great a tendency to summarize the clinical material presented, though in all fairness to the author it must be admitted that the syndromes are so diverse as to defy classification in many instances. The syndromes of the long and short circumferential vessels are much less convincing than that of the paramedian artery, and the latter is difficult to differentiate from the syndrome of ordinary hemiplegias. The monograph will be found useful to both clinicians and pathologists.

Hypnosis and Suggestibility: An Experimental Approach. By Clark Hull. Price, $3.75. Pp. 405, with 71 illustrations. New York: D. Appleton-Century Company, Inc., 1933.

The state of generalized hypersuggestibility which may follow the hypnotic procedure is, in Hull's opinion, the only remaining characteristic of the "once imposing aggregate known by the name of hypnosis." He believes that the other characteristics, which were described and have long been maintained on the basis of clinical study, all fall before an experimental attack. These include rapport, catalepsy, heightened sensibility, the relating of hypnosis to true sleep, on the one hand, and to pathologic conditions of hysteria, on the other, and the consideration of hypnosis as a state of dissociation.

Much of the experimental work was carried out by Hull and his students at Yale. On the whole, it is convincing, but there are many fundamental questions, as Hull notes, which cannot be answered without further evidence. One of these is the question why the particular stimulations used in inducing the hypnotic trance should produce generalized hypersuggestibility. There are experiments which show that such an increase in suggestibility does not result from direct waking suggestions and others which show that it does not depend on the beliefs of the subject about hypnosis and the power of the hypnotist.

In Hull's opinion, direct or prestige suggestion, the form which must be considered in connection with hypnosis, is different from indirect, nonprestige suggestion. This opinion is based on differences in certain characteristics of prestige and nonprestige suggestion but is not yet supported by conclusive experimental evidence. Prestige suggestion is concluded to be a habit phenomenon in which the subject's symbolic processes remain passive, thus giving the "symbolic processes (ideas) of the *experimenter* a kind of right of way to the control of the subject's movements."

The book is well introduced by presentations of the elementary phenomena of hypnosis and the facts of direct waking suggestion. There is also a brief historical survey, together with references to the earlier beliefs on specific aspects of the problem. Hull's concentration on the new experimental approach, however, leaves him relatively little space for clinical findings, either early or modern. Such concentration was necessary in order to bring the problem of hypnosis out of the realm of the pseudoscientific, but many aspects of the problem yet to be solved undoubtedly require a more extensive combination of the experimental and clinical data.

Textbook of Abnormal Psychology. By Roy M. Dorcus and G. Wilson Shaffer. Price, $4. Pp. 389, with 4 plates. Baltimore: Williams & Wilkins Company, 1934.

Perhaps this might be regarded as the first formal textbook on abnormal psychology that approaches clinical psychiatry closely. Dorcus and Shaffer have intentionally prepared it for the "needs of advanced students in psychology, particularly medical students who desire more psychological information." A foreword by Knight Dunlap comments on the critical balance of the book and the beginning of an epoch by its publication. An additional foreword by Dr. Ross McClure Chapman is complimentary. It brings out the psychiatric point of view, however, that the psychologist must be warned against the practice of psychiatry. All in all, the book seems to be a textbook of psychiatry written entirely from a psychologic point of view. Schizophrenia, manic-depressive psychoses and involutional melancholia are listed as functional psychoses. Various theories as to the cause of different clinical psychoses and, particularly, psychoneuroses are presented fairly. The field of psychoanalysis, particularly freudian theories, has had little effect on this presentation. The last chapter is on psychotherapy and occupies forty pages, in which are outlined psychotherapeutic procedures from suggestion, catharsis, desensitization and reeducation, through psychoanalysis to general psychotherapeutic aids which might be used in environmental changes.

The book is well written, easy to read and understandable. The first section on sensory and motor disorders is technical and contains much neurophysiology, with emphasis on abnormalities or irregularities in such physiology.

For the present, the book is probably as good a synthesis of psychology and psychiatry as might be desired. As a book for students it will prove useful. However, through oversimplification psychoses and other psychiatric conditions are made to seem too psychologic, too functional and too easily subject to treatment by purely psychologic methods. The value of the material will therefore depend entirely on how it is presented to students and under what influences they study.

It is thought that not enough indirect emphasis is placed in the text to discourage students of psychology from attempting clinical practice because of the interrelation of psychology and psychiatry. A fine bibliography is appended, as well as a good index.

Practical Neurological Diagnosis with Special Reference to the Problems of Neurosurgery. By R. Glen Spurling, M.D. Price, $4. Pp. 225, with 99 illustrations. Springfield, Ill.: Charles S. Thomas, Publisher, 1935.

This book should prove an excellent answer to the badly felt need for a manual of neurologic examination suitable for students and for physicians outside the special field of neurology. It presents in a clear, orderly, logical and simple way the essential steps in taking a neurologic history and in making a proper survey of the patient. Accompanying each item there is a concise discussion of the anatomy and physiology involved. There are appended chapters on the dynamics and serology of the cerebrospinal fluid, and on roentgenography, including methods and interpretation of roentgenograms of the skull and spine, ventriculography and encephalography, and the use of opaque mediums.

While admittedly presenting his material from a neurosurgical point of view, Spurling has succeeded in furnishing an adequate guide to any practitioner of medicine for a thorough study of any of his patients who presents symptoms referable to the nervous system. The outline, if used generally, would obviate many of the sources of confusion which result in oversight and misinterpretation. If one were to make suggestions for further editions of the book, they would be in the direction of amplification of the significance of positive findings and of pointing out more forcibly that neurologic phenomena may be the presenting evidence which leads backward to a primary diagnosis, such as that of hypertension, bronchogenic carcinoma or pernicious anemia. It would also be well to add a chapter on glandular pathology as related to the central nervous system, notably that involving the pituitary body.

The book does not pretend, however, to be other than a manual of examination. As such it fulfils its function admirably, and it should be in the possession at least of all interns, and of practitioners who call in consultants, as a model to be followed in the acquisition and assembling of requisite data.

L'angiographie cérébrale. By Egas Moniz. Price, 90 francs. Pp. 328, with 192 illustrations. Paris: Masson & Cie, 1934.

This book is a real contribution to the medical literature. One cannot help admiring the clear and systematic manner with which the subject is presented. Egas Moniz first presents an unusually complete analysis of the main blood supply to the brain in normal persons. The anatomic considerations are enhanced by many lucid illustrations taken from his collection of more than six hundred instances of patients who received injections of thorium dioxide solution.

After demonstrating the normal findings, the author presents a long series of cases of tumors of the brain in which angiography had been employed. The histories are outlined, and the roentgenograms demonstrating the vascular changes considered diagnostic of lesions in various portions of the brain are presented. In many instances the brain itself is pictured, which allows easier interpretation of the cerebral angiogram. Cerebral aneurysms are beautifully visualized by the method. The marked difference in the vascularity of meningiomas and astrocytomas is demonstrated, and the difference in their roentgen appearance makes it possible to determine the nature of the lesion prior to operation.

The monograph seems complete in every aspect of the particular subject with which it deals and is amply illustrated by one hundred and ninety-two reproductions.

Book Notices

The 1934 Year Book of Neurology, Psychiatry and Endocrinology. Edited by Hans H. Reese, M.D.; Harry A. Paskind, M.D., and Elmer L. Sevringhaus, M.D. Price, $3. Pp. 782. Chicago, The Year Book Publishers, Inc., 1934.

"The 1934 Year Book of Neurology and Psychiatry" is characterized first by the fact that for the first time in many years this volume is not under the direct editorship of Dr. Peter Bassoe, who developed it to such a standard of excellence that it has become a necessary part of every neurologic library. Dr. Bassoe's hand, however, is seen in the new volume, which maintains the excellence of accomplishment which characterized the volumes of which he was editor.

The new volume is divided into three sections—those on neurology, psychiatry and endocrinology. The section on endocrinology is a welcome addition to the other two and serves to emphasize for neurologists and psychiatrists the importance of this aspect of neurophysiology to their respective specialties. The portions on neurology and psychiatry are well edited and abstracted. On the whole, the articles chosen for abstracting constitute the more important contributions to the neurologic and psychiatric literature. The arrangement of the abstracts in the portion on neurology follows in general the outline developed in previous editions. Practically all the subjects reviewed have a critical editorial comment by the editor, which is useful and in some instances valuable.

The volume can be highly recommended to all who are interested in neurology and psychiatry. It is a useful handbook for quick reference and maintains well the standard created by its former editor.

Mental Deficiency Nursing (Simplified). By O. P. Napier Pearn, Deputy Medical Superintendent, Cane Hill Hospital, London. Price, $2. Pp. 289. Baltimore: William Wood & Company, 1934.

This excellent comprehensive and well written little book constantly makes one wonder at the amount and variety of information contained in two hundred and eighty-nine pages. In addition to dealing with the nursing of mental defectives, it contains chapters on general nursing, first aid, hygiene and an explanation of terms. One might almost say that it is a nursing manual and Godey's "Ladies Book" combined.

Symptoms are listed under special headings, with notes as to what the nurse should do and, equally important, what she should not do. There are some illustrations of various types of mental defectives. There are all sorts of handy information for the nurse; instructions concerning medicine are given, and even such subjects as cookery and methods of admitting and receiving new patients are considered.

The book is in a handy small edition and may conveniently be slipped into one's pocket. It is decidedly worth while and should be of value to nurses engaged in the handling of those mentally defective.